CARDIAZOL

Registered Trade Mark

ANALEPTIC

and

general STIMULANT,

more particularly of

CIRCULATION AND RESPIRATION

Completely soluble in water and lipoids
Exceptionally rapid action
Wide therapeutical range
Absence of unpleasant side-effects

1938

KNOLL A.-G., MANUFACTURING CHEMISTS,

LUDWIGSHAFEN - on - RHINE

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PREFACE

The object of the present book is the compilation, in handy form, of all the clinical publications and some of the more important literary references on the subject of Cardiazol which has now played its part in therapy for over 10 years. The book offers a complete survey of the experiences gained and recorded in a great many branches of medicine. The section dealing with clinical experiences, therefore, covers not only the more usual therapeutic fields of indication for Cardiazol but is completed by references also to the "rare" indications. The practitioner is thus enabled quickly to find information on any question concerning Cardiazol as far as it has been touched upon in the literature. Moreover, new therapeutic uses for the remedy may suggest themselves to the attentive reader.

Our book begins with a short history of Cardiazol followed by an exhaustive description of its chemo-physical and pharmacological properties. The principal section consists in a full account of all the clinical experiences collected up to the end of 1936. The Cardiazol combinations on the market—"Cardiazol-Quinine", "Cardiazol-Dicodid Drops" and "Cardiazol-Ephedrine" —are likewise discussed in detail. A separate section goes into the question of the numerous further possibilities of Cardiazol combination. The list of authors and that of indications at the end of the book complete the work. —

definite antagonist, but it has proved its power also against other narcotics (Pernocton*, ether, chloroform, etc.). Cardiazol is able briefly to interrupt (for the purpose of food administration) twilight-sleep artificially induced in catatonias by hyoscine-morphine or Luminal*, and the same applies to Rectidon*-twilight-sleep induced in morphinists.

The *rousing of narcotized patients* generally demands fairly high doses of Cardiazol. Frequently several c.c. require to be given by slow intravenous injection, combined with intramuscular or subcutaneous injections. No definite scheme can be laid down; the dosage must be adapted to the gravity of a case. In the event of motor restlessness, e.g., slight twitching occurring, the intravenous injection is best stopped. Spasms which may follow over-dosage need cause no apprehension. The Cardiazol spasms are harmless and disappear quickly without any trace of damage. They never develop into paralytic manifestations. This is of the greatest importance for the reason that the convulsive dose must often be nearly approached and even reached.

The harmlessness of the Cardiazol spasms is responsible for the use of the remedy for convulsion therapy of schizophrenia. Large intravenous injections have been found to produce epileptic attacks. With 1000 injections there has not been a single case of damage. On the other hand, definite remissions were secured in 40% of all cases.

The rousing action and convulsive action are, above all, cortical manifestations. Excitation of the cerebral cortex by Cardiazol has also been definitely proved by means of action currents. Cardiazol dilates the cerebral vessels and increases the blood perfusion of the brain, thus creating more favourable

Cardiazol is a potent *analeptic*, yet free from danger even in high dosage. In the main its action develops along the central nervous organs.

The basis for the clinical use of a medicament can only be established by pharmacological tests. Only the latter are able to lead to clear, even though not always final, views. It is not our purpose, however, to adduce scientific proof of the analeptic properties of Cardiazol in a survey of the numerous and accurately obtained experimental results but to present to the medical reader a clear picture of the advantages and effects of our preparation as established by clinical experience. It will hardly be regarded as a defect if the separate effects are incapable of sharp delineation, seeing that the final and total result is the only factor of interest to the physician in the treatment of his patients.

Cardiazol is an eminent *rousing agent*. Extensive clinical observations furnish unequivocal proof that, if given in sufficiently large doses, Cardiazol shortens the narcotic state considerably and often abruptly ends it; the patients awake, open their eyes and are able to converse. This fact is of great practical importance for the reason that anæsthesias induced by the now frequently employed injection and rectal narcotics are not controllable. With Cardiazol, serious damage, always liable to arise from narcoses, can be prevented. It stands to reason that not every form of narcosis can be influenced to the same extent, for the various narcotics also have their various points of attack. In the case of Medinal*, Evipan* and Avertin*, Cardiazol is a

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and vessels cannot be strictly judged apart and combined forms of collapse also occur.

Central hæmodynamic collapse is vasomotor paralysis. Its simplest form, a fainting attack, is marked by sudden loss of consciousness, pronounced pallor, a small, frequent pulse and extraordinarily low blood-pressure. Similar conditions obtain in collapse following loss of blood. No longer purely hæmodynamic is the frequent post-operative collapse where, apart from paralysis of the vasomotor centre, an escape of plasm from the blood and increased nitrogen excretion have already set in.

Pure forms of peripheral plasmatic collapse occur after burns, traumata and histamine shock. Serious loss of plasma from the blood to the tissue (cf. pulmonary œdema) here cause a thickening of the blood and impairment of the oxygen supply through diminished permeability.

The *states of collapse most frequently seen at the bedside* in infectious diseases, peritonitis, food-poisoning, etc., generally have their cause in a debilitated circulation and not in primary cardiac disturbances. Although vasomotor paralysis plays an important part here, peripheral factors are frequently accessory. It is for the physician to judge in each case whether the central hæmodynamic form preponderates, or the peripheral plasmatic form. Without a searching examination it will frequently be impossible to decide the point accurately.

Cardiazol has, above all, proved of excellent value in infectious diseases as a "circulatory restorative" of sure action. This description, whilst characterizing the chief action of Cardiazol is, nevertheless, too narrow because Cardiazol represents a general centrally acting analeptic.

of the apparently drowned. Even where artificial respiration and cardiac massage succeed in setting the impaired circulation going to some extent, it is still of importance that Cardiazol should reach the heart, and thence the brain, as quickly as possible. A subcutaneous injection, which must be given in any case, only represents a first-aid measure which, in slight cases, may prove sufficient. In grave cases, however, even an intravenous injection of 1–3 c.c. may not suffice alone. Here it is best to inject the Cardiazol, together with about 50 c.c. physiological salt solution, into a brachial vein. Even where circulatory activity has apparently ceased, this procedure will often produce instantaneous resuscitation.

The successful action of Cardiazol in *collapse* may be made clearer by a brief survey of the respective mechanisms of the various forms of collapse. Fundamentally, there are two forms of collapse: the central, hæmodynamic, and the peripheral, plasmatic. The cause of collapse is generally conceived to be a decline in the amount of the circulating blood. Somewhere blood is retained in the depots and thus withheld from the circulation. Too little blood is offered to the heart which, seen through the X-ray screen, therefore always appears small. The veins of the neck are empty, due to peripheral vasomotor insufficiency. Collapse-like circulatory disturbances resulting from primary cardiac failure are less frequent. In these, the blood is held up in the dilated cardiac cavities in which the pressure increases, the afferent veins being filled to capacity. A fall in blood-pressure, tachycardia, dyspnœa and cyanotic pallor, also a swollen liver and oliguria, are common to both conditions. Often it is difficult to form a clear opinion respecting the origin of a state of collapse: in estimating circulatory activity, heart

ved. Sovereign remedies of this kind are adrenaline and kindred substances which constrict the vessels peripherally, thereby voiding the blood depots and raising the minute volume. An excessive rise in the blood-pressure in this connection is generally undesirable because of the extra strain thrown on the heart. All other results follow secondarily through improved blood access and oxygen supply to the nervous centres. What is unattainable by this treatment is a heightening of the excitability of the central nervous organs above normal values. Where a typical peripherally acting circulatory analeptic also produces a rousing effect under certain conditions, the effect is generally only of very brief duration.

Where indicated, *general nervous central analepsis is combined with peripheral "circulatory analepsis"*. Cardiazol-Ephedrine was introduced for that purpose. The synergist action of the combination will often produce excellent results although experience shows that in the generality of cases Cardiazol alone does all that is required.

These observations apply to collapse in general, i.e., without special consideration of the peculiarities of peripheral plasmatic collapse. The causal therapy of the latter form would, above all, demand a lowering of the capillary permeability for blood plasma. Whether Cardiazol is able to effect this is, for the moment, an undecided question although numerous clinical observations point to very good effects of the remedy also in this form of collapse. The increased permeability of the capillaries for oxygen engendered by Cardiazol no doubt plays an important part here.

In connection with the regularization of the circulation by Cardiazol, the question of an *action on the heart* requires ventilation.

If, in the *treatment of collapse*, the main object is mobilization of the blood held up in the depots so as to stimulate the circulation by raising the cardiac minute volume and to enhance the oxygen supply for the purpose of revitalizing the organism, the methods open to us are, fundamentally, of two kinds:

1. *An analeptic in the strict sense of the word* is used, i.e., a remedy which raises the excitability of the nervous centres, thereby stimulating their activity in a direct manner. This results in a deepening of the respiration which alone improves the mechanical side of the circulation, facilitates oxygen assimilation and oxygen transport. The effect on the cerebral cortex leads to awaking and to voluntary movements supporting the circulation. The activity of the vasomotor centre increases simultaneously, constricting the small blood-vessels and voiding the depots so that the heart receives more blood. An increase in the blood-pressure is of no significance: the virtue of an analeptic consists in its increasing the volume of the circulating blood, i.e., a raising of the minute volume. If the circulation is thus indirectly restored to a normal state, the further stimulation of all other functions follows as a matter of course. A further advantage, however, consists in the greater responsiveness of the central nervous organs which endures for some time. In that sense Cardiazol acts as a general analeptic acting on the central nervous system, with an indirect influence on the circulation.

2. The attempt is made to exert a direct primary influence on the circulation and thus to place a "*circulatory analeptic*" *function* in the narrow sense into the foreground. For that purpose we require a remedy with an action on the peripheral vessels, seeing that in collapse the heart is not, generally speaking, invol-

administered digitalis preparation has had time to develop its influence. A mixed Cardiazol-digitalis therapy, moreover, increases the susceptibility of the heart to digitalis, and where strophanthin is given, its sometimes unfavourable influence on impulses and conductivity is neutralized. Thus are Cardiazol and digitalis not competing remedies, but synergists. In cases of digitalis and strophanthin idiosyncrasy, a protracted Cardiazol medication is a practical way out of the difficulty, always of great benefit and never injurious.

The dilatation of the coronary vessels of the heart by Cardiazol justifies its use in *angina pectoris*, as practised and appreciated by many authors. Intravenous injections are, generally speaking, best avoided also in acute attacks, the subcutaneous route being usually adequate. In cases associated with myocardial debility, continuation of the treatment for some time with Cardiazol liquid, given several times daily, is advocated. It may without hesitation be continued for months as there is no risk of either cumulation or habituation. In one case nearly 1000 c.c. Cardiazol has been given in the space of $3^1/_2$ months with good results. Combinations with other remedies, such as morphine or Dilaudid (Knoll), which may occasionally be requisite, are always compatible.

The manifold use of Cardiazol as a *general excitant* requires no further justification after what has gone before. Even here it is not merely the "tonic effect on the circulation" which is in question, although its regulatory effect on the circulation is always a marked feature; for Cardiazol, owing to its general central nervous attack, also stimulates respiration, the activity of other subcortical stations and the functions of the cerebral cortex and

Clinical evidence is unanimous on the point that in numerous cases of heart disorders (myocarditis, myodegeneratio, valvular defects, etc.) Cardiazol does, as a matter of fact, exert a very favourable influence. The reason, on the one hand, is that it regulates congestions present in cardiac decompensation, thereby easing the heart's work. With the circulation, central cardiac and peripheral vascular factors form an entirety, incapable of strict separation. This, of course, would not furnish proof of a Cardiazol effect on the heart, but experienced clinicians and physicians are no doubt correct in their assertion that Cardiazol has a stimulating influence on cardiac activity, as it is certain to-day that Cardiazol dilates the coronary vessels, thereby creating the prerequisite for improved cardiac metabolism and cardiac activity. This positive inotropic action is indirect, but older experiments which had already suggested a direct positive inotropic heart action of Cardiazol, have recently been confirmed and extended. Of especial importance is the fact that Cardiazol administration never results in cardiac paralysis.

Even though Cardiazol, in accordance with clinical experience, stimulates cardiac activity indirectly and no doubt also directly, the use of digitalis in serious chronic and acute cases cannot be dispensed with despite the considerable improvement in the condition of heart patients effected by Cardiazol. The Cardiazol action is fugitive and there is no cumulation, for which reason the remedy is naturally unable to achieve the same lasting results as the cumulative digitalis medicaments, even if given in large and continuous dosage. In conditions of decompensation, however, the rapid onset of the Cardiazol effect is able to give excellent *immediate results, of great assistance until the simultaneously*

administered digitalis preparation has had time to develop its influence. A mixed Cardiazol-digitalis therapy, moreover, increases the susceptibility of the heart to digitalis, and where strophanthin is given, its sometimes unfavourable influence on impulses and conductivity is neutralized. Thus are Cardiazol and digitalis not competing remedies, but synergists. In cases of digitalis and strophanthin idiosyncrasy, a protracted Cardiazol medication is a practical way out of the difficulty, always of great benefit and never injurious.

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the spinal marrow. In addition, and in contrast with many other analeptics, Cardiazol supports the activity of the motor apparatus, a fact evidently based on a stimulation of the peripheral nerve-endings.

The *tonicising effect* is much utilized in a great variety of infectious diseases. Circulatory debility is fought with Cardiazol. Prior to operations it is given as a prophylactic and favourable results are on record also in pulmonary tuberculosis. At high altitudes, Cardiazol causes the unpleasant symptoms of mountain-sickness to disappear quickly, exhausted climbers recovering their elasticity. It seems highly probable that, beside the general analeptic effect, the greater permeability of the small blood-vessels for oxygen plays a decisive part. Cardiazol has also frequently proved of excellent value in balneology as a preparatory tonic. It will be seen that the field of indications for Cardiazol is extremely wide.

A *heightened diuresis* caused by Cardiazol and often observed clinically, is probably for the most part a sequel to circulatory regularization.

Finally, there is the influence of Cardiazol on the *respiratory organs* which demands attention. The successful influence on pulmonary œdema and the excellent expectorant action are no doubt mainly connected with the general control of the circulation and the consequent improvement in pulmonary perfusion. But another important factor is that Cardiazol resolves bronchial spasms, for which reason it has become known as an excellent, rapidly acting remedy in bronchial asthma and laryngospasms. The simultaneous administration of adrenaline or similar substances will not, in many cases, be readily dispensed with and the

introduction of Cardiazol-Ephedrine takes this point into account. The combination results in a potentialized action owing to its simultaneous central and peripheral attack.

The various publications and reports on which this survey of the Cardiazol effects from their practical aspects is based will hereafter be fully discussed. Our introduction merely intends to give a brief review of fundamental points and the principal advantages.

It is our hope that this book will prove a useful source of information and a welcome adviser to the physician regarding his therapeutical procedure.

KNOLL A.-G. Scientific Dept.

HISTORY

The history of the origin of Cardiazol has recently been told in interesting detail by its discoverer, Prof. *K. F. Schmidt*, Heidelberg, and we give the particulars in the following.

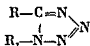
It is not very easy to determine whether Cardiazol owes its discovery to research having a definite therapeutic objective in view, or to a mere accident.

The self-imposed task had certainly been to derive water-soluble substances from camphor and other ketones of the camphor group which, whilst exhibiting a change in physical properties, would yet retain the therapeutic properties of camphor. Success at first remained in abeyance. In working directly towards the aim in question the endeavour was to leave the camphor ring system and its characteristic groups (carbonyl, isopropyl) intact as far as possible. Like the majority of real inventions or discoveries in the chemical field, that of Cardiazol also came about along the circuitous route of investigations based on purely scientific problems, in which considerations respecting practical utility played no part. The latter could thus only emerge at a much later stage on the basis of the findings then available.

The investigations which led to the discovery of the catalytic dissociation of hydrazoic acid (N_3H) into nitrogen (N_2) and the imino radical (NH) had no practical aims in view, no more than the resulting questions concerning the nature and mutability of

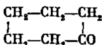
the NH-, the "imino radical", which is indeterminable in its unchanged state.

The influence of the latter on ketones produced a reaction, surprising to the chemist, inasmuch as the otherwise stable carbon chain of the ketones is broken by the imino radical which intrudes into the chain next to the carbonyl group (CO). This principal reaction is accompanied by another in which, apart from the imino radical, an entire molecule of hydrazoic acid acts on the ketone, with liberation of water, so that in all 4 nitrogen atoms are introduced. The products thus obtained from a variety of ketones all belong to the group of tetrazoles, ring combinations of the type



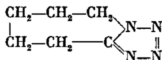
in which R and R_1 represent different organic groups in accordance with the basal ketone.

Further lateral processes, partly of considerable extent and of a still more complicated nature, at first made it difficult to reach a conclusion as to the method to be adopted in the synthesis of the end-products in a pure form; also *ring-form ketones* showed themselves amenable to these transmutations. For the subsequent experiments the choice did not, however, fall on camphor because of its complicated structure and ready inclination to changes and decomposition, but cyclohexanone, with its much simpler structure, was selected as a substitute for camphor. It has the following formula:



It is now established that, without adopting this chemical principle, the discovery of Cardiazol would not only have been missed, but neither would the scientific developments have been achieved in the camphor group.

Apart from three other substances, which also engaged the interest of the chemist, cyclohexanone yielded pentamethylentetrazol (Cardiazol) in small amounts. The constitution of Cardiazol:



was at first assumed only by analogy and later found its confirmation in splitting-up and decomposition reactions. Its formation from the six-membered cyclohexanone results from the extension of the ring by a nitrogen atom to a seven-membered compound, under simultaneous evolution of the five-membered tetrazol ring.

Seven-membered rings are in themselves rare. The combination of one of these with the tetrazol ring had not previously been known. Thus Cardiazol was the first representative of a new group of substances and, as its simplest member, also forms its basal compound.

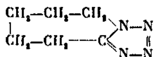
The striking physical properties of the substance, its unusual stability and resistance to chemical reagents, its ready solubility in water and practically all organic solvents, including lipoids, and, finally, its complete neutrality and, therefore, non-irritant properties of its solutions, comprised all the desiderata for a therapeutic agent. Whilst these special physical properties of a new basal substance suggested physiological investigation, there

existed also certain, though indeterminate, chemical relations with active derivatives of the camphor molecule containing a combined seven- and five-membered ring system.

The physiological test thus resulted as the last link in the investigations to establish the properties of the new substance. *If the latter was handed to the pharmacologist with the request* to test it for camphor effects, this may appear strange in view of the scanty relations between the two substances. But the *evolutionary history explains matters.*

CHEMICAL AND PHYSICAL PROPERTIES

Cardiazol (Knoll) is pentamethylentetrazol:



It is a white, crystalline powder, with a faintly bitter taste; melting point 58–59° C., softening slightly before melting. Small amounts of Cardiazol are practically odourless. Large amounts have a characteristic cherry-wood smell. Owing to its low melting point, Cardiazol in powder form conglobates on storage, without, however, undergoing any chemical change or impairment of its activity.

It is very readily soluble in water and most organic solvents. The solutions are neutral. The aqueous solutions can be sterilized without experiencing any decomposition and the substance is infinitely stable, whether stored in solid form or in solution. Of

its derivatives the combination with mercuric chloride, melting at 175° C. and with difficulty soluble in cold water, is characteristic; it is produced by the addition of a cold, saturated solution of mercuric chloride to an aqueous solution of Cardiazol, which immediately yields a crystalline precipitate.

BACTERIOLOGY

Experiments carried out by *v. Angerer* showed that germs implanted in a 1 and a 10% Cardiazol-saline solution neither multiplied nor continued to live; in other words, they were killed. It must be added that this bactericidal effect is weaker in the presence of nutrients. Involuntary tainting of the solutions destined for therapeutical injections with nutrient material corresponding to the 2% bouillon added in experiments, is, of course, excluded in practice. Bacterial growth in Cardiazol solutions is, therefore, impossible unless there is gross negligence.

PHARMACOLOGY

The fundamental pharmacological investigations of Cardiazol were carried out by *F. Hildebrandt*[1] and his disciples. If its similarity to camphor is frequently stressed, the intention is to emphasize the appearance of a remedy now really possessed of all the favourable therapeutic properties formerly ascribed to camphor (probably wrongly). No similarity exists between the chemical structures of the two substances. *Pharmacologically,*

Cardiazol has its place rather in the picrotoxin group (*Buding*) or, more generally speaking, in the group of analeptics with a central point of attack (*Gremels*, *F. Hildebrandt*[1], *Zipf*).

The most conspicuous effects of Cardiazol in the case of normal and undamaged animals are those on the

Nervous System.

The first manifestations are heightened restlessness and excitability. With larger doses, clonic spasms ensue after the preliminary stage described. These spasms greatly resemble picrotoxin convulsions (*Camp*).

Schoen found that the character of the convulsions is not greatly altered by extirpation of the cerebrum. *Bertha*, on the other hand, was unable to establish genuine clonus in decerebrated rabbits (*Trendelenburg*'s rhythmical motorial manifestations, *unrelated* to normal and, more particularly, to locomotor movements). He observed types of convulsion being none other than rhythmical, normal movements (scratching and locomotorial movements). From this one may safely conclude an excitation of the subcortical centres whence the impulses issue. At the same time, an excitation of superior centres in the undamaged animal cannot be dismissed. That excitation is indeed proved by the experiments of *M. H. Fischer* and *Löwenbach*. *Koch* observed that the initial convulsive manifestations can be suppressed by physiological stimuli (pressure on carotid sinus).

The *spinal marrow* itself also represents a point of attack of Cardiazol. *Blume* regards the stimulus-receptive part of the reflex arc as the locality of attack whereas *Koll* sees the latter in the motorial part.

Action on Reflexes.

The influence of Cardiazol on reflexes, as dependent on dosage and method of application, has been closely investigated by *Schoen* who made use of Magnus' methods. The excitant effects of Cardiazol are functionally in contrast to the paralyzing effects of the narcotics. Cardiazol is able to rouse an organism plunged in deep, almost lethal narcosis. The greater the dose of the narcotic given and the more profound the narcotic state, the more Cardiazol is required to terminate that state. Vice versa, Cardiazol convulsions caused by excessive doses or the too rapid application of intravenous injections, can be resolved by relatively small amounts of a suitably chosen narcotic. The antagonism certainly varies more or less considerably according to the kind of narcotic used. It is most marked in the case of narcotics having the greatest number of points of attack in common with Cardiazol. This appears to apply, for instance, to Medinal* and Cardiazol, but Cardiazol has also proved a very efficacious rousing agent in connection with a great many other narcotics, e.g., ether, chloroform, hypnotics of the fatty acid group or barbiturates, i.a., Avertin*, Amytal*, Eunarcon*, Pernocton*, Evipan*, etc., in experiments on all kinds of animals (mice, rats, guinea-pigs, rabbits, cats, dogs, monkeys) even where the animals had been poisoned by doses otherwise bound to produce lethal results. (*Adam, Albus, Barlow, Biehler, M. H. Fischer* and *Löwenbach, Fulton* and *Keller, Gros, Gros* and *Haas, Kohlhoff, Kohn* and *Jacobi, Koppanyi, Linegar* and *Dille, Lendle, Mehl, Morris* and *Eastman, W. Müller, v. Nyári, Russu* and *Sparchez, Schwab* and *Jung, Tartler, Zipf.*) Relating their investigations of Veronal*

poisoning, *Gros* and *Hofmann*, as well as *Hofmann*, draw attention to the fact that during the later stages a peripheral circulatory disturbance develops by the side of the purely central paralysis and that in this condition ephedrine is a happy complement to the Cardiazol medication. (*Mannini*'s results with Cardiazol-Ephedrine were less satisfactory but the inadequate number of his trials seems to furnish an explanation for his findings.) *Barlow*, who has in a large number of cases tested the Cardiazol-Ephedrine effects in hypnotic poisoning from doses otherwise unfailingly lethal, regards the combination as one of the most efficient restoratives. It should be mentioned that *Zipf* and *Hoppe* have established a detoxicating action of Cardiazol also in connection with local anæsthetics (Novocain* and Larocain*).

A part-effect of this general centrally excitant action of Cardiazol is the influence on the

Vomiting Centre

observed by *Schwartz*. The vomiting centre can be paralyzed by hypnotics such as diethylbarbituric acid, etc., to an extent where even apomorphine is no longer able to induce vomiting. This paralysis can, by Cardiazol, be so counteracted that apomorphine can again produce its emetic effect.

Heat Centre.

Another point of attack possessed by Cardiazol is the central heat-regulating mechanism. In rabbits, a fall in the temperature of $1-1^1/_2$° C. is seen after administration of 0 02 gm. per kilo. Since

correspondingly large doses are not used in human therapy, a similar effect cannot conceivably arise in the latter.

Of greater therapeutic importance is the excitation of the

Respiratory Centre

as produced by Cardiazol already in small doses and even in normal animals. According to *Zunz*, Cardiazol is a direct excitant of the respiratory centre, however administered; the excitation is observed after oral administration (*Hildebrandt* and *Voss*) as well as after subcutaneous and intravenous injection (*Hildebrandt, Schoen, Schübel* and *Gehlen*); it is naturally very marked also after injection into the 4th ventricle (*Jánossy*). The effect is particularly demonstrative if the respiratory centre has been previously paralyzed by morphine or hypnotics (*Behrens* and *Reichelt, Braams, Henderson* and *Sparks, Hildebrandt, Jackson, Lendle, Schoen, Toscano Rico, Trendelenburg*). The influence of Cardiazol on Pernocton* narcosis in the dog has been closely studied by *E. A. Müller*. He found the spontaneous lessening of the narcotic state accompanied by increased energy expenditure. Respiration and circulation improved proportionately. The relation of respiratory volume to energy expenditure, as well as the respiratory quotient, remained constant the while. Where, however, the narcotic depth was diminished through Cardiazol, the respiratory volume increased more through the ensuing greater respiratory depth than through the greater respiratory frequency. The relation above referred to rose to a higher level, as did the respiratory quotient, signs of excitation of the respiratory and circulatory centres. The exhaustive experiments carried out by *Eichler* and *Klein* on rabbits in Avertin*

narcosis show the great therapeutical range of Cardiazol. It is somewhat wider with rapid injections (11—12) than with slow injections (9—10). The action on the respiratory mechanism (diaphragmatic and thoracic movements) in the case of Cardiazol is always an influence on inspiration, excepting with threshold doses where that influence is not in evidence.

The Cardiazol effects as such, and also from the point of view of the drug's antagonism to morphine, have been investigated by *Steininger* and *Gaubatz* quantitatively also in respect of the human respiratory centre. The results have been confirmed by *Stanton Hicks*.

Another manifestation of the general excitant influence of Cardiazol is its action on the

Vasomotor Centre.

This action had previously been recognized and investigated by several workers (*Flaum*, *Hildebrandt* and *Eichler*, *Junkmann* and *Stross*, *Palme*, etc.). In many of these experiments the action may possibly have been indirect, via the respiratory centre; nevertheless, a direct attack at the vasomotor centre is placed beyond a doubt by *van Esveld*'s results. The last-named author found that Cardiazol, in contradistinction to all the other analeptics examined by him, occupies a separate position in so far as it was often found able to increase susceptibility of the vasomotor centre to the CO_2 stimulus. This condition of heightened excitability lasted considerably longer than the other (more fugitive) acute Cardiazol effects. *Raab*, on the other hand, mentions that, in human practice, he has observed a decrease of vasomotor centre excitability (see also *Raab* and *Friedmann*).

It might be expected that the Cardiazol action would find expression in a rise in the

Blood-pressure.

It should, however, be remembered that in a normal organism an increase in the blood-pressure is countered by a whole series of opposing regulations. This is seen also in the case of Cardiazol, especially as, according to *Zunz* and *Tremonti* as well as *Zancan*, the carotid sinus which plays the prinicipal part here (*Palme*), remains uninfluenced by the remedy. It is indeed a fact that, in normal animals, constancy and often even a lowering of the average pressure has been observed (*Hildebrandt* and *Eichler*, *Goworow* and *Speranskaja-Stepanowa*). Conditions are different in the case of the pathologically lowered blood-pressure: here a rise in the pressure must probably be expected in all circumstances, as also in collapse on a peripheral basis (*Leffkowitz*, after chloroform; *Koch* and *Palme*[1], after histamine; *Oettel*, after acetylcholine; *Flaum*, after papaverine overdosage). In this connection a very interesting observation was made by *Koch*: a fall in the blood-pressure caused by narcosis, or also by a histamine infusion, can be corrected by a continuous Cardiazol infusion. At the height of the rise, the carotid sinus, however, exhibits a different behaviour. Excitation in narcosis does not result in a lowering of the pressure whilst excitation from a histamine infusion produces a marked decline. *v. Bergmann jr.* has shown that Cardiazol injections, repeatedly given at regular intervals to a narcotized animal, result in a uniform and lasting rise in the blood-pressure during a practically unlimited period (see also *Zinnitz* and *v. Bergmann jr.*).

The behaviour of the

Average velocity of the circulation

has been studied by *Bansi*, *Kalinke* and *Rohrlich*. In circulatory insufficiency, with marked retardation of the peripheral blood-stream, as seen, e.g., in pneumonia and severe cyanosis, an accelerating action of Cardiazol of about 2 hours' duration was observed.

Action on the heart?

In view of the dependence of cardiac activity on the periphery it cannot be denied that Cardiazol exerts an indirect action on the heart. On the one hand, an increased blood supply by itself leads to an improvement in the cardiac function; on the other, the coronary vessels experience even passively a better perfusion where the arterial blood-pressure is raised. The simultaneously improved respiration supplies the heart-muscle with more oxygen and thus enables it to do better work (*Gremels*[1]). In addition, *E. A. Müller*[1] observed an active dilatation of the coronary vessels from Cardiazol medication. The reader may here be reminded of the adrenaline liberation proved by *Bömer* (via the splanchnic nerves) whereby an indirect improvement of the cardiac function is also secured.

On the question of a direct Cardiazol action on the heart opinions continue to differ. Positive results obtained with the hearts of frogs (often absent owing to varying and seasonable susceptibility) and with the *Langendorff* heart (*Bürgi* and *Gordonoff*, *Hendrych*, *Hildebrandt*, *Sanders*, *Schütz*, *Stross*, *Strube*, *Takabe Tadashi*, *Watt*) are to-day rejected by many as not convincing (*Gremels*[2]). In experiments ordered according to *Starling*,

the absence of toxic effects on the heart, even of supertherapeutic doses of Cardiazol, has indeed invariably been established; not, however, a positive influence (*David* and *Vareed, Gollwitzer-Meier, E. A. Müller*[2]). It would, nevertheless, be premature to dismiss the idea of a direct Cardiazol action on the heart; let us remember that in the *Starling* preparation the heart works under highly unphysiological conditions. We must leave it an open question whether improved methods will not, after all, be able to prove a direct action of Cardiazol on the heart-muscle.

But it must always be remembered that "cardiac action" is not synonymous with "digitalis action". Although a number of workers (*Biehler, Eismayer* and *Quincke, Fahrenkamp, Freund* and *König*) emphasize the qualitative analogies to digitalis, far-reaching differences are nevertheless present; above all, there is no cumulation. Thus it will never be possible to effect a "digitalisation" of the heart with Cardiazol; on the contrary, misconceived experiments of this sort must be warned against (*Löhr, Flaum, v. Nyári*).

The positive inotropic action observed by *W. H. Stein* and *M. H. Fischer*[1] on the pseudo-tendinous fibre, the moderator band of the sheep's heart, is obtained with Cardiazol concentrations of a strength which leaves *Stein*'s conclusions open to doubt. Of much greater practical significance doubtless is the Cardiazol action on the

Striated skeletal musculature,

closely investigated by *M. H. Fischer*[2]. This author found that Cardiazol has a favourable influence on the fatigued striated muscle to which it restores susceptibility to central impulses.

Whether this effect is attributable only to improved perfusion of the musculature or to an influence on the motorial end plates (even curare paralysis has been interrupted) is at present an open question.

We must further mention the influence on the

Smooth musculature

which is relaxed by Cardiazol; *M. Baur* has proved this action on his nerve-free, purely smooth-muscular amnion preparation. In smooth muscle preparations such as the small intestine, Cardiazol lowers the tonicity but little, in contradistinction to the bronchial musculature where the action is considerably more marked, particularly where the musculature is convulsively contracted. This is *Januschke*'s opinion, based on clinical experience. Experimental proof has been supplied by *Biehler*.

A few words remain to be said about

Absorption and excretion.

Cardiazol is very readily soluble in water, but, at the same time, also easily soluble in lipoids. It is not surprising, therefore, that the difference in the time of onset of action after subcutaneous and intravenous injections is very small (*Hildebrandt*[1]). The intensity of effect after subcutaneous administration reaches relatively high values, i.e., about half those of intravenous injections (*Schoen*). Absorption by the intestinal canal is also most favourable: it is quantitatively almost complete and the process already begins in the stomach (*Schoen*, *Voss*). Since, however, the Cardiazol stream enters the organism at a slower rate than after intravenous injection, it is necessary to administer about four

times the intravenous dose per os in order to obtain the same effect. It may be concluded from the almost complete absorption of Cardiazol that it undergoes very little change in the liver through which it must pass at least partly. This is also *Ridder's* conclusion after experiments with the surviving liver of the frog and the cat. Given orally, the Cardiazol action is, in accordance with the slower reception in the blood, not quite so powerful but, on the other hand, much more protracted.

In regard to the final destiny of Cardiazol in the organism, no more can be said than that its action diminishes after some time. The explanation is the disappearance of the Cardiazol owing either to storage, destruction or detoxication. According to *Hildebrandt*[2], the speed of detoxication in the case of an average convulsive dose of 11 mgm. per kilo amounts to 0·85 mgm. per kilo per minute. The value of 0·83 mgm. per kilo per minute, established by the 10 hour trials made by *Barker* and *Levine*, agrees well with the foregoing. Measured by the convulsive result, the relation between concentration of the intravenously injected solution, within the limits of 20%–2%, and a time of about 40 seconds, corresponds exactly to the rule $c \cdot t =$ const. With lower concentrations, requiring more time for their injection, we find marked deviations which also explain why the injection of 2 doses of 1 c.c., the second given shortly after the first, does not produce the effect of 2 c.c. injected in 1 dose and why very slow injection of doses productive of convulsions, if injected rapidly, does not produce convulsion (*Biehler*).

Nothing definite is known about the mechanism of Cardiazol detoxication. Only slight traces of unchanged Cardiazol are excreted in the urine after therapeutic doses.

CLINICAL EXPERIENCES

I. General

Methods of administration, dosage, onset of effect, duration of effect

The onset of the Cardiazol effect has been found to vary but little with intravenous, intramuscular and subcutaneous injection, an advantage evidently due to the unusually rapid absorption of Cardiazol which is so very readily soluble in water as well as in lipoids. Clinical and experimental experience of many years has, however, established definite methods of application as the most suitable for specific indications. Certain, although not invariably valid, rules for the use of one or the other method of administration have thus been laid down.

Intracardial injections of Cardiazol (1–2 c.c.) will not be resorted to except in desperate cases. Where, despite the absence of clinical signs, some little cardiac and circulatory activity exists, the promptest possible conveyance of Cardiazol to the nervous centres may save life.

Injection by the *intravenous* route is of much greater significance and it appears to be the method of choice in all urgent, life-threatening, cases. In principle, Cardiazol injections into the vein must be performed at the slowest possible rate. Since the preparation disappears in the organism relatively quickly, it is better to repeat the injection at intervals of 15, 30 or 60 minutes rather than to give too large an amount in one dose. Very slow

and repeated injections enhance the Cardiazol tolerance without diminishing the efficacy of the preparation.

1, 3, and even 5 c.c. (rarely more) may be given pro dosi, according to the severity of a case, but the amount of an intravenous single dose cannot be schematically fixed. It is, generally speaking, highest in cases of poisoning and of rousing from narcoses (3 c.c. and even up to 5 c.c.). Close observation of the patient during the slowly performed injection generally discovers the correct moment for the discontinuance of the injection; signs of motorial restlessness are the determining factor. Intramuscular or subcutaneous Cardiazol injections may, however, follow immediately and up to about 5 c.c. may be injected without hesitation.

Serious cases of poisoning, incidents during narcosis, dangerous collapse, apparent death from drowning, threatening respiratory paralysis, asphyxia, etc., form the field of indications for intravenous Cardiazol therapy. In serious circulatory insufficiency and collapsed veins, an injection with about 40 c.c. saline solution or glucose solution is the treatment recommended. The Cardiazol then reaches the heart very promptly and is thence conveyed to the vital centres, with the sequel of a full and rapid action.

Intravenous Cardiazol injections demand caution in states of spasmophilia (illuminating gas- or carbon monoxide-poisoning, apoplexies, tetany, occasionally meningitis, cocainism, morphinism, etc.). In these cases, intramuscular or subcutaneous injection deserves the preference because a too high concentration is avoided. Intravenous injection should also be shunned in severe *angina pectoris.* It is unsuitable no doubt also in operations on

the brain since the acute dilatation of the cerebral arteries through Cardiazol may give rise to hæmorrhages. In infants and young children, the motorial effect even of fairly large doses of Cardiazol (3 c.c.) is minute.

Cardiazol is, moreover, very suitable for intravenous *continuous drop-infusions.*

There is no notable difference between the degree of action of *intramuscular* and *subcutaneous* injections. The choice may, therefore, be determined by extraneous circumstances. The onset of action generally occurs after 5–8 minutes and the effect reaches its peak after about 15 minutes. The usual single dose amounts to 1 or 2 c.c. but it may be increased to 5 c.c. according to requirements. There is no need for special measures of precaution. The field of indications concerns the cases in which a radical and rapid, but not absolutely sudden, action is necessary (minor grades of collapse, fainting attacks, heatstrokes, acute circulatory debility, pulmonary œdema, bronchial asthma, intoxications, grave infectious diseases, etc.). To bring on prematurely born children, the subcutaneous injection of glucose infusion with 1–2 c.c. Cardiazol is recommended. The Cardiazol injections may be given several times daily, and even hourly, without hesitation.

Cardiazol liquid (20 drops several times daily) and the Cardiazol tablets (1 tablet 3–4 times daily) serve for the *oral* administration of the remedy. The single dose and the daily oral dose may likewise be considerably increased where circumstances demand it. The onset of action ensues relatively promptly (within about 10 minutes) unless absorption is impeded by faulty circulation, congestions or other causes. The action persists from

1–3 hours so that it is easy to maintain a lasting effect by the repeated administration of small doses.

In view of the above, internal doses of Cardiazol are best suited to achieve a lasting tonic effect on the circulation as well as an excitant and roborant action. Unfavourable after-effects need not be feared. In this manner, the circulation may be controlled, fatigue combated, physical and mental capacity increased, climatic changes and tolerance of varying altitudes facilitated, and so forth. Cardiazol may also be taken prophylactically without hesitation. The oral medication, furthermore, represents an efficacious adjuvant to injections and may take their place for the continuance of the Cardiazol treatment. The complete innocuousness even of large doses opens up a wide range of uses for the oral application of Cardiazol in daily life, in view of its potent action. Continuous administration harbours no dangers nor does it entail diminishing efficacy. Cardiazol does not incommode the stomach.

Cardiazol can also be administered rectally, and suppositories containing 0 1–0·2 gm. Cardiazol powder, or small enemata with 1–2 c.c. Cardiazol liquid added, may be recommended.

In desolate cases where all blood transportation has ceased, an intracisternal (suboccipital) injection of 0·4–0·5 c.c. Cardiazol may still be tried.

No secondary effects

Even where injections are repeatedly given, no undesirable results, such as cumulation, cerebral symptoms, renal irritation, intestinal paralysis or habituation, will occur. Cardiazol injections, given every 1–2 hours during 2 days, produced no unfavourable

effects at the sites of injection. Even on protracted administration, oral Cardiazol medication never produces gastric discomforts.

Pulse

After the administration of Cardiazol, *the previously* small, fluttering, generally barely palpable, pulse quickly becomes fuller and more powerful. The pulse frequency returns to normal, the irregularities due to abnormal stimuli often disappear. At the height of the action, the tension of the pulse is satisfactory and may be likened to the digitalis pulse.

Respiration

Where the respiratory centre is damaged, Cardiazol will produce a conspicuous stimulation and deepening of the respiration.

Blood-pressure

It was frequently found that the administration of Cardiazol is followed by a rise in the maximal pressure and a decline in the minimal pressure; in other words, the blood-pressure amplitude is extended.

Expectoration

Numerous authors stress the favourable influence of Cardiazol on expectoration (in pneumonia, etc.). In many cases, the use of any particular expectorant in addition to Cardiazol is, therefore, unnecessary.

II. Special

INTERNAL MEDICINE

A. Cardiac and Circulatory Disturbances

(a) Acute circulatory debility

Krehl says that circulatory disturbances from any cause, and developing either slowly or quickly, are equally well acted upon by Cardiazol which also influences respiration. *Leschke* speaks of Cardiazol as one of the most efficient agents with which to combat circulatory debility. *Mayr* has also used Cardiazol in acute circulatory debility, invariably with success. The action sets in earlier than in the case of camphor but is not so persistent. According to *Lange*, Cardiazol is of value especially in cases of serious, acute circulatory debility in which a rapid onset of action is the main point. Where the pulse was impalpable and an injection into the collapsed veins impossible, a subcutaneous injection of Cardiazol generally restored the pulse within a few minutes whilst the congested veins filled again. Also *Pochmann* has observed the prompt and certain action of Cardiazol especially in acute and subacute cardiac and circulatory insufficiency.

(b) Chronic circulatory debility

Gabriel points out that Cardiazol is indicated not merely in acute but also in chronic circulatory disturbances. *Bottari*'s experiences likewise concern cases of acute cardiac insufficiency and chronic circulatory depression.

(c) Collapse, vasomotor debility

Krehl says that Cardiazol, given intravenously in collapse, is positively astonishing in its action. At all events, the action on the circulation was much more potent and prompt than after an injection of camphorated oil. According to *Ruef*, the value of Cardiazol is greatest in acute disturbances due to sudden failure of the entire circulation, especially in states of collapse. *Nonnenbruch* also remarks that Cardiazol and similar products are excellently capable of stimulating the respiratory and vasomotor centres in states of collapse. *Hemmerling* observed quick improvement in the perfusion of the skin and the visible mucous membranes soon after the administration of Cardiazol, nor was the regulating effect of a Cardiazol injection on respiration less conspicuous. Dyspnœa disappeared after 10 minutes, breathing became quieter and more regular, severe cyanosis and thoracic oppression were often instantaneously abolished by intravenous injections. *Rausche*'s experiences in the treatment of collapse also show that the action of Cardiazol is surprisingly rapid. *Leffkowitz* shows in his investigations of the behaviour of the splanchnic vessels in collapse that Cardiazol is able, by constricting the blood-vessels, to send the blood collected in the abdomen back into its normal paths and thereby to increase the volume of circulating blood and to raise the blood-pressure. He describes a case of collapse following repeated serious uterine hæmorrhage in which a subcutaneous Cardiazol injection restored the circulatory function within 1–2 minutes, removing all acute danger. *Rauter* has always seen prompt action from Cardiazol (in combination with skin stimulation and, occasionally, artificial respiration) in sudden conditions of collapse. Many of his patients had lost a

great quantity of blood, respiration had already ceased and the pulse was no longer palpable. In cases of this nature he invariably gave Cardiazol intravenously (2 c.c.). Within 2–4 minutes the organism recovered visibly and normal respiration, a regular and strong pulse and clearing of the sensorium followed. Occasional relapses were with certainty combated by a repetition of the intravenous Cardiazol injection. In one case of alarming unconsciousness the patient awoke immediately after administration of 3 c.c. Cardiazol as from a sleep. On the strength of his experience *Rauter* regards Cardiazol as *eminently suitable to save life* in the various alarming states of the circulatory system, in view of the rapid absorption and excellent tolerance of the remedy. Injurious or merely uncomfortable secondary effects have never been observed, whether from normal or supernormal doses. *Dubois-André* recommends Cardiazol on account of its tonicising action on the circulatory and respiratory centres, more particularly where collapse threatens and for protracted treatment. According to *Claass*, the use of Cardiazol in states of collapse is becoming much more common on account of its immediate effect on the pulse which grows fuller and better within a few minutes whilst the blood-pressure rises and soon reaches normal values. The rise in the blood-pressure is owing to a constriction of the capillaries in the splanchnicus region; this causes the mobilization of a considerable volume of blood which enters the circulation (a kind of *internal blood-transfusion*). *Ito* advocates intracardial injections of Cardiazol combined with adrenaline, in collapse, cardiac paralysis, etc. *Holm* and *Eggers* are also in favour of intracardial injections being given apart from adrenaline, or even in the place of the latter.

Cardiazol is amongst the medicaments recommended by

Hoff in *vasomotor paralysis. Domarus* also advocates the use of Cardiazol for the purpose of raising the vasomotor tone through its centrally excitant property.

Bansi, *Kalinke* and *Rohrlich* found that Cardiazol effects an improvement in the velocity of the blood stream and in the blood supply in the venous section, greatly lessening the risk of circulatory failure.

The main indication for Cardiazol, according to *Moller*, is the centrally conditioned vascular insufficiency with the equally centrally conditioned respiratory insufficiency as found, in the first place, in narcotic poisoning; but Cardiazol, according to clinical experience, has its therapeutic value also in circulatory insufficiencies of other origin where the blood supply to the central nervous system (and thus to the respiratory and vasomotor centres) is reduced. According to *Flaum*, the principal indication for the Cardiazol therapy is toxic, infectious vasomotor paralysis occurring in the course, or as a sequel, of infectious diseases. He is in the habit of giving Cardiazol prophylactically, whilst the circulation is not yet involved, in all serious, acute and chronic infections, more particularly pneumonia, typhoid fever, etc. Further indications are the toxic states (morphine, hypnotics, carbon monoxide), which lead to paralysis of the centres situated in the medulla oblongata; also asphyxia occurring during narcosis and after operations, states of collapse following serious loss of blood or psychic or physical traumata. In cardiac insufficiency, however, Cardiazol appears to be useless unless the disorder is associated with peripheral circulatory disturbance. The recognition of the camphor preparations as drugs with peripheral (= vascular) action is emphasized also by *D. Scherf*. It is

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(e) Cardiac debility, heart disorders (valvular defects, decompensation), Congestive œdemata, etc.

In certain cases of *cardiac debility* (angina pectoris, pericarditis) *Morawitz* had better results with Cardiazol than from digitalis. The effect being only transient, a first injection must, where the depressive symptoms persist, be followed by another after 2–3 hours. In *Hasenfeld*'s opinion, combinations of digitalis with Cardiazol and similar preparations are a valuable enrichment of the therapy in high-grade cardiac debility. *Determann* also advocates the use of Cardiazol in addition to strophanthin where cardiac debility develops. Caution in respect of the intravenous use of digitalis bodies (strophanthin) in acute, absolute cardiac debility in obese persons is advised by *David* who advocates the simultaneous use of Cardiazol (Strophanthin. comp.*). *Polevski* gave Cardiazol in serious cases of ischæmic or non-congestive cardiac debility. With correct dosage, the remedy can be given for many weeks without fear of toxic effects. In regard to the treatment of *cardiac collapse*, *Wiechowski* expressed the opinion that Cardiazol and other water-soluble analeptics are not able to raise the cardiac function (minute volume), but that they are well able to stimulate the vasomotor centre powerfully and thereby to counteract cardiac collapse. He adds that these remedies are not suitable for the treatment of primary cardiac debility.

According to *Pochmann*, Cardiazol is a powerful adjuvant in digitalis treatment of chronic *heart disorders*, more particularly if given orally. The simultaneous use of Cardiazol and strophanthin has been found especially advantageous. *Mayr* advocates the use of 10 drops Cardiazol, twice to thrice daily for 3 days, in chronic, slowly progressing heart disorders, from the very

also stated by *Fröhlich* that Cardiazol and camphor substitutes have the character of general circulatory stimulants rather than of genuine cardiacs, for which reason they cannot, and must never be, used in the place of digitalis preparations. *Arnovljević* is also of opinion that analeptics of the Cardiazol type have no direct influence on the cardiac function and are, therefore, not suitable for use in chronic cardiac debility with insufficiency symptoms. *v. d. Velden* points out that in cases of primary cardiac insufficiency, excitants (including Cardiazol) are inefficacious. *Schoen* regards as the chief field of indication for circulatory analeptics (Cardiazol, etc.) actual or developing collapse, not, however, cardiac insufficiency; nevertheless, the inseparability of disturbances of the cardiac and circulatory periphery renders an exact delimitation of the therapeutic indications impossible.

(d) Vascular block, air embolism

Januschke records his observations according to which Cardiazol has a vasodilator action, useful, above all, in cases of general or localized vascular block such as may occur in neurotic states of debility and collapse or as sequels of a too powerful vascular effect exerted by adrenaline in asthma; in vasoconstriction of arteriosclerosis (hypertension, vascular atony and respiratory disturbances due to oblongata anæmia; angina pectoris); in vascular spasms produced by caffeine and ergotine; in chronic nephritis associated with hypertension. The vasodilator action of Cardiazol was especially conspicuous where the vasoconstrictive drug caffeine had been given previously.

W. Neumann gave lobeline and Cardiazol (amongst other remedies) in *air embolism*.

regarded as particularly useful also by *Risché* since relatively little strophanthin needs to be given for the attainment of a full therapeutical effect. Cardiazol is, moreover, able to abolish or prevent poisoning by too large strophanthin doses (ventricular fibrillation). There is evidence, therefore, that Cardiazol can render the administration of strophanthin a safe measure. *Akil Muhtar* and *Besim Ruşen* state that for some years they have given *ouabain in combination with Cardiazol* ($^1/_4$ mgm. ouabain + 1 ampoule Cardiazol) in the mixed syringe, intravenously, in serious cases of asystolia. They have gained the clear impression that this method often produces superior results. *Haddad* is another writer expressing the view that the Cardiazol and ouabain combination is able to exert a favourable influence on heart disorders at first regarded as hopeless, and that the ouabain therapy has found an extension through Cardiazol.

In decompensated *cardiac defects* with cardiac and peripheral disturbances, *Eppinger* recommends, in addition to the typical cardiacs, the use of circulatory remedies, e.g., Cardiazol, etc. *Lange* has had good results with Cardiazol in chronic circulatory debility both in myocardial insufficiency and insufficiency due to valvular defects. This refers also to cases in which digitalis was not tolerated. *Rosin* is strongly in favour of Cardiazol treatment of *cardiac decompensation in its initial stage. Hippe* was able to raise tension and quality of the pulse with Cardiazol in grave conditions of decompensation, the influence on blood-pressure and respiration being likewise favourable. In many cases there was evidence that Cardiazol also effected an enhancement of the effect of digitalis preparations inasmuch as compensation was attained in less than the usual time and could, subsequently, be maintained

beginning of the digitalis medication and until the digitalis (Digipuratum) action has fully developed, above all where œdema tends to develop. The adaptation of the circulation is then more satisfactory and the heart, in a sense, increases its susceptibility to digitalis.

Fahrenkamp commences the treatment of chronic heart cases with intravenous daily doses of 1 c.c. Strophanthin. comp.* (0·25 mgm. strophanthin + 0·1 gm. Cardiazol). The addition of the Cardiazol results in the same effect being achieved with 0·25 mgm. strophanthin as is otherwise attainable only by 0·5 mgm. strophanthin. If well tolerated, the initial dose is maintained until the major symptoms of insufficiency have disappeared. With continued improvement, the intervals between the injections are continuously lengthened. If after an interval of 5–6 days there is no increase in weight, rectal digitalis therapy can be resorted to [generally with 0·8 mgm. Verodigen*, twice daily, or 0·1 gm. Digipuratum (Knoll) twice daily], with 10–20 drops Cardiazol 3 times a day in addition. In his trials with the *combined strophanthin-Cardiazol therapy*, *Fahrenkamp* observed that *the transient, sudden fall in frequency no longer occurred.* This refers also to cases of bradycardia in arrhythmia perpetua (pseudo-heart-block). In 20 very grave cases of this kind in which the resort to strophanthin treatment seemed to involve certain risks, its combination with Cardiazol prevented all impairment of cardiac stimuli and conductivity. A notable fact is also that where strophanthin and Cardiazol are given in combination, a full effect can be obtained with a sub-threshold strophanthin dose. In *Fahrenkamp*'s opinion, the reason lies in definite synergism. The treatment of circulatory debility with a combination of Cardiazol and strophanthin is

regarded as particularly useful also by *Rische* since relatively little strophanthin needs to be given for the attainment of a full therapeutical effect. Cardiazol is, moreover, able to abolish or prevent poisoning by too large strophanthin doses (ventricular fibrillation). There is evidence, therefore, that Cardiazol can render the administration of strophanthin a safe measure. *Akil Muhtar* and *Besim Ruşen* state that for some years they have given *ouabain in combination with Cardiazol* ($^1/_4$ mgm. ouabain + 1 ampoule Cardiazol) in the mixed syringe, intravenously, in serious cases of asystolia. They have gained the clear impression that this method often produces superior results. *Haddad* is another writer expressing the view that the Cardiazol and ouabain combination is able to exert a favourable influence on heart disorders at first regarded as hopeless, and that the ouabain therapy has found an extension through Cardiazol.

In decompensated *cardiac defects* with cardiac and peripheral disturbances, *Eppinger* recommends, in addition to the typical cardiacs, the use of circulatory remedies, e.g., Cardiazol, etc. *Lange* has had good results with Cardiazol in chronic circulatory debility both in myocardial insufficiency and insufficiency due to valvular defects. This refers also to cases in which digitalis was not tolerated. *Rosin* is strongly in favour of Cardiazol treatment of *cardiac decompensation in its initial stage. Hippe* was able to raise tension and quality of the pulse with Cardiazol in grave conditions of decompensation, the influence on blood-pressure and respiration being likewise favourable. In many cases there was evidence that Cardiazol also effected an enhancement of the effect of digitalis preparations inasmuch as compensation was attained in less than the usual time and could, subsequently, be maintained

with Cardiazol alone. Also *Fahrenkamp* finds that the slighter cases of cardiac insufficiency (in ambulant patients) are treated with quicker results if Digipuratum (Knoll) and Cardiazol are given simultaneously. In the treatment of gravely decompensated heart patients who cannot be left without morphine preparations, he regards a combination of Cardiazol with Dicodid (Knoll) or Dilaudid (Knoll) as useful. *Wollheim* differentiates two kinds of decompensation: plus- and minus-decompensation. In minus-decompensation, *digitalis is contraindicated whereas substances* inducing a fuller peripheral circulation (Cardiazol, etc.) are indicated.

Hippe found that a heightened diuresis follows the use of Cardiazol in *congestive œdemata*, the effect being due to a stimulation of the circulation. *Castex, Sacón* and *López Ramírez* observed an increase in diuresis of 50–100% in heart patients with extensive œdemata and oliguria. *Bottari* observed a *considerable increase in diuresis* in cases of water-retention in the tissues. In one case of circulatory decompensation associated with dyspnœa, very extensive œdemata and copious pleural exudation, intensive Cardiazol treatment was resorted to after thoracocentesis: the urine excretion, previously 1000 c.c. on an average, rose to 4000 c.c. on the following day and during the next few days kept in the neighbourhood of 2500–3000 c.c. *Fleckseder* mentions the excellent diuretic effect of Cardiazol injections in cardiac dropsy.

(f) Heart-block, Stokes-Adams' attacks, coronary thrombosis, cardiac infarct

Cardiazol is recommended by *Hubert* as an excitant in *heart-block*. Excitants, especially Cardiazol, during the existence of heart-block, are considered imperative also by *Lange*. *Bischoff*

gave Cardiazol amongst other remedies in a case of complete heart-block.

Herz administers Cardiazol internally in *Stokes-Adams' attacks*.

Behr uses Cardiazol, etc., in *coronary thrombosis*, as does *Bontscheff* in acute attacks of that disorder to counteract cardiac debility. *Donath* is in favour of giving Cardiazol and similar remedies as vascular tonics (several times daily)in the treatment of acute coronary occlusion with a marked decline in the blood-pressure so as to abort impending collapse. *Lepehne* is also of opinion that the use of cardiacs and vascular tonics (e.g., Cardiazol), apart from strophanthin, is indispensable in cases of this description. *Friedländer* administers high percentage glucose solutions with Cardiazol, etc., in threatening pulmonary œdema. In urgent cases, caffeine and intermediate doses of centrally excitant circulatory remedies (Cardiazol, etc.) are recommended by *Frank*. *Hasenfeld* favours the combination of sleep-inducing agents with vasomotor remedies, e.g., Cardiazol, to ensure the hypnotic action in disorders of the coronary vessels with hypertension.

Bickel and *Mozer* mention Cardiazol among the medicaments suitable for the relief of cardiac paralysis in thrombotic *cardiac infarct*. Also *Schüssler* gives Cardiazol, etc., in cardiac infarct in the place of digitalis to counter threatening insufficiency. Angina pectoris, associated with infarct, is treated by *Schüler* with Cardiazol, etc.

(g) Angina pectoris

Siebeck counsels the administration of Cardiazol during actual angina pectoris attacks where the pulse is not satisfactory and where are signs of myocardial debility. Also *Leschke* regards cardiacs

indicated in cardiac debility and, during an attack, gives the preference to Cardiazol (the dose repeated twice or thrice according to requirements). It is an acknowledged fact that Cardiazol renders good services also in angina pectoris during the intervals between attacks. *Cobet* recommends the administration of analeptics (e.g., Cardiazol) in angina pectoris where there is a decline in the blood-pressure. After fruitless efforts with digitalis, *Boing* treated an angina pectoris patient with myocardial debility with Cardiazol, achieving success by means of large doses (the daily maximum being $8 \times 25 = 200$ drops, in the acute attack frequently also an additional 2 and even 3 c.c. Cardiazol subcutaneously and intravenously in 10 c.c. glucose solution). Notwithstanding the high dosage and protracted period of administration, there was no habituation, i.e., impaired action. A fresh dose of Cardiazol is recommended before the effect of the last has completely subsided. In a case of the gravest form of angina pectoris, *Feld* injected 1 c.c. Cardiazol intravenously six times within 6 hours, regardless of the ensuing convulsions, the final result being deep sound sleep and an increase in the pulse rate to 40. *Zimmermann* speaks of Cardiazol as a valuable adjuvant to other remedies in angina pectoris. He relates a case of grave organic angina pectoris which remained refractory to all imaginable remedies but improved promptly on 3 c.c. Cardiazol, injected subcutaneously. He recommends Cardiazol (liquidum) amongst other remedies for the relief of the daily anginous discomforts. The use of Cardiazol in angina pectoris as an analeptic, or *prophylactic of threatening collapse*, is advocated also by *Kulbs*, *v. Romberg*, *Fürbringer* and *Wollheim*. *Krehl* advises a trial with intracardial injections of Cardiazol, etc., in sudden apparent death from angina pectoris.

Leibowitz observed that intramuscular injections of 1 ampoule Cardiazol, given at the height of a stenocardial attack, will, after a few minutes, completely abolish the pain in the chest and arm and that the collapse-like aspect of the morbid picture undergoes a decided change. In the slighter, subchronic forms of stenocardia, he recommends the administration of Cardiazol-Dicodid in doses of 10 drops twice daily. Confirmation of the *favourable effects of Cardiazol combined with Dicodid (Knoll), or also Dilaudid (Knoll)*, in stenocardia, is furnished by *Hopmann*.

Kaiser mentions the case of a patient who collapsed during an attack of angina pectoris after a morphine injection. The heart gave the impression of being in a state of fibrillation. An intravenous Cardiazol injection, quickly given, was immediately successful. *L. Stein* advises caution respecting the use of opiates and recommends the simultaneous administration of caffeine or Cardiazol; also *Zak* is in favour of administering *circulatory tonics (e.g., Cardiazol) simultaneously with morphine. Hemmerling* found that Cardiazol has an *antispasmodic* action in angina pectoris attacks. The use of the preparation appears to be particularly indicated in the graver forms. Patients experience immediate alleviation which frequently renders the subsequent administration of a sedative superfluous. *F. Meyer* recommends intramuscular or intravenous injections of Cardiazol in stenocardial attacks for the purpose of quieting the spasm first of all. *Neu* had good results in angina pectoris with a *combination of 0·1 gm. Cardiazol + 0·04 gm. papaverine hydrochloride.*

In grave cases of *status anginosus* and cardiac infarct, *Volhard* advocates the use, not of digitalis, but of Cardiazol. The administration of cardiac stimulants already during the early

stages of status anginosus is advocated also by *Kisch* (i.a., subcutaneous injections of Cardiazol).

(h) Asthma cardiale

According to *Hemmerling*'s and *Ito*'s experiences, Cardiazol is of excellent value in cardiac asthma. *Zak*, i.a., recommends Cardiazol in combination with morphine (0·01—0·02 gm.) for the treatment of acute attacks; nightly doses of Cardiazol in pulmonary œdema as a sequel to an asthma attack; the same also in cardiac asthma of elderly people (with bronchitis and emphysema), adding that the remedy is naturally no substitute for digitalis. *v. Romberg* points out that an evening injection of Cardiazol combined with morphine is useful in preventing the tormenting state experienced by patients suffering from nightly recurring attacks. Correspondingly good results have been seen by *Neu* from Cardiazol in combination with papaverine (0·1 gm. Cardiazol plus 0·04 gm. papaverine hydrochloride). Enemata with Euphyllin*, caffeine and Cardiazol are recommended by *Přibram* where cardiac asthma causes discomforts like oppression, portal vein congestion and oliguria.

(i) Arteriosclerosis, hypertension, apoplexy, etc., coronary sclerosis, nephrosclerosis

Bruno has used Cardiazol (1 tablet, 3—4 times daily) in the treatment of *arteriosclerosis*, more especially in the presence of subacute and chronic disturbances, and found that the product diminishes the heightened pulse frequency as well as the raised blood-pressure, harmonizes systole and diastole and exerts a decided influence on the vascular centre. In arteriosclerotic myocardial degeneration, improvement of the grave states of de-

compensation has been observed. *Moeues* says that in arteriosclerotic degeneration of the heart-muscle, Cardiazol brings out the action of digitalis preparations, be they given simultaneously or later, where the digitalis doses concerned are ineffectual without the Cardiazol addition. *Treu* mentions a case of grave arteriosclerosis (true goose-neck arteries) in which a subcutaneous administration of 1 c.c. Cardiazol given in the evening exerted a favourable vascular action which lasted through the night. *Neu* gives Cardiazol also in cases of slight decompensation in aortic sclerosis and essential hypertension. With this medication, he achieved, within an average of a week, regression of the discomforts, lessening of the sensation of thoracic oppression, cerebral pressure, irritability, also improvement of the symptoms of decompensation, decline of the raised blood-pressure, a stronger and more regular pulse. *B. A. Schwartz* records successes with Cardiazol (alone or in combination with digitalis) in chronic congestive cardiac debility and heart-muscle damage, mostly of arteriosclerotic, hypertensive origin. In acute states of debility (hypotension) in arteriosclerosis, *Fahrenkamp* favours the administration of Cardiazol-Ephedrine, or else Cardiazol + Digipuratum (Knoll). In the acute stage, an intravenous injection of Cardiazol + Digipuratum (Knoll) may have a truly life-saving effect. *Árpád* recommends excitants such as Cardiazol in arteriosclerosis during attacks of angiospasm with reduced blood-pressure.

B. Kraus suggests a combination of the hypotonics with Cardiazol in *hypertension* treatment. *Estapé* is another author recommending the use of analeptics (Cardiazol, etc.) in hypertension treatment, especially where a sudden marked drop in pressure occurs.

Mattirolo advocates (i.a.) the intravenous injection of Cardiazol for the treatment of sequelæ of *apoplexia cerebri*. *Franck* uses camphor, Cardiazol, etc., where heart failure is to be feared. *Attinger* describes a case of apoplexy in which the patient's condition grew alarming through marked anæmia of the extremities, superficial respiration, coma, grave pulmonary œdema and a very rapid pulse. It was not expected that the patient (a woman) could live more than an hour or two. Cardiazol + digitalis brought her round with astonishing speed. The damage to the circulation caused by vasomotor and respiratory failure and failing expectoration was most favourably acted upon by Cardiazol in a very short time. *Hippe*, writing on the subject of apoplexy (and chronic interstitial nephritis), says that Cardiazol visibly improves the general condition.

According to *H. A. Hofmann*, Cardiazol renders good services as an antispasmodic in *hypertensive migraine* and *vertiginous conditions*. *Dietrich* reports good results from Cardiazol in migrainoid headaches.

The administration of analeptics, more particularly Cardiazol, should, according to *Schoen*, precede other treatment in *coronary sclerosis* with attacks of cardiac asthma or angina pectoris.

In *nephrosclerosis*, *Hildebrandt* treats the more serious states of decompensation with intravenous injections of strophanthin (in small doses) plus Cardiazol and a 20% grape sugar solution.

(h) Arrhythmia, tachycardia, ventricular fibrillation

With the aid of the electrocardiogram, *Bottari* was able to prove that, in *arrhythmia*, the administration of Cardiazol results in a decline of the pulse frequency and in improvement or aboli-

tion of extra-systolic arrhythmias. *Ito* ascribes a particularly pronounced action to Cardiazol in cardiac arrhythmia and fibrillation. *Kirkowitsch* administers quinidine in total arrhythmias invariably in combination with heart tonics, including Cardiazol, for the purpose of regularizing the cardiac function. *Kern* describes a case of myocardial insufficiency with serious arrhythmia. The patient, a woman, had received three daily doses of 8–10–12 drops Cardiazol, according to requirements, for 9 years. Whilst at first she was often bedridden for months, she was subsequently able to get up and also to take short walks. Every attempt to substitute other remedies for Cardiazol or to discontinue the treatment, immediately resulted in renewed debility with arrhythmia; digitalis was not tolerated at all.

A. Hoffmann recommends Cardiazol in *paroxysmal tachycardia* in elderly people left with cardiac debility after collapse. In the treatment of paroxysmal tachycardia, *Schilder* always gives camphor or Cardiazol prior to artificially provoked vomiting (vagus irritation via the vomiting centre). *Birk*, *Lethaus* and *Plügge* give a Cardiazol injection in paroxysmal tachycardia before every Doryl* injection.

Parade gives the preference to Cardiazol in *ventricular fibrillation.*

(l) Cardiac neuroses

Moeices finds the administration of Cardiazol tablets (suitably combined with bromides) very useful in cardiac neuroses. Cardiazol has also been given by *Serafinski* in cardiac neuroses with much success. *Géronne* has been able to procure relief to sufferers from various forms of cardiac neurosis by giving them small

amounts of Cardiazol (or similar excitants). Disturbed circulatory co-ordination, for instance, was improved (see also page 153).

(m) States of exhaustion, hypotension, etc.

Moewes tried Cardiazol as an analeptic in nervous cardiac debility following *conditions of exhaustion*, and found it superior to caffeine. *Licci* prescribes Cardiazol as a circulatory and respiratory restorative in exhausting illnesses of long standing, i.a. also in nervous exhaustion, depressions and organic enfeeblement of psychasthenics, tumorous cachexias, etc. *Turyn* gives Cardiazol wherever myocardial exhaustion demands the administration of a restorative. The remedy rendered good services also in sudden adynamia, shock, etc. *Calcaterra* has repeatedly given Cardiazol in cases of marked vascular debility (in infectious diseases of long standing, states of marked emaciation, grave hæmorrhages, etc.), his results being thoroughly favourable (see also page 153).

Pichler observed that Cardiazol raises the blood-pressure in *arterial hypotension*. *Castex, Sacón* and *López Ramírez* refer to Cardiazol as particularly valuable in cases requiring stimulation of the cardiovascular tonus and an elevation of the blood-pressure. *H. Baur* also recommends Cardiazol (i. a.) for the improvement of the vascular tone in hypotension.

Cardiazol and Cardiazol-Ephedrine are among the remedies recommended by *Arnovljević* as useful in *orthostatic hypotension*.

(n) Pericarditis

Deicher and *Tiedke* say that analeptics, such as caffeine and Cardiazol, should always be kept at hand for pericarditis patients in case of possible circulatory disturbances.

B. *Disorders of the Respiratory Organs*

(a) Bronchitis

Januschke reports that the stenotic bruits occurring in acute and chronic bronchitis are abolished or diminished by Cardiazol (3×1 c.c. subcutaneously). The remedy is also able to act as an expectorant by the solution or loosening of spastically held lumps of secretion in the bronchia. According to *Gordonoff*, Cardiazol has an indirect expectorant action owing to its excitant effect on the respiratory centre. *Krehl* recommends Cardiazol, as an alternative to camphor, in cardiac and circulatory disturbances following acute bronchitis. For grave cases he advocates the intravenous use of strophanthin.

(b) Bronchial asthma

Januschke finds that 1 c.c. Cardiazol, injected subcutaneously three times daily, abolishes bronchial stenosis in certain forms of bronchial asthma promptly and completely. *Zengerle* says that, amongst cardiacs, Digipuratum (Knoll) and Cardiazol render the best services in bronchial asthma. *Lange* likewise speaks of the frequently favourable action of Cardiazol in bronchial asthma with debility of the right heart. *Werdersheim* recommends Cardiazol for its supporting action on the heart function. *Gutmann* gives it in cases in which disturbances of the cardiac or vascular systems exist in any form. *Ijiri* has had valuable results from Cardiazol + adrenaline (subcutaneously) in asthma cases. *Dubois-André* states that Cardiazol, in combination with morphine, Dilaudid (Knoll) and adrenaline, is able to suppress and prevent asthmatic crises. Its tonic effect on the circulation prevents the secondary vascular dilatation (collapse, tremors, palpitations) evoked by adrenaline.

Exceptionally good results have been obtained in bronchial asthma with "Cardiazol-Ephedrine", the combined preparation (for details see page 215).

(c) Asphyxia, dyspnœa, emphysema

Among preparations suitable for the treatment of *asphyxia*, *Binet* mentions Cardiazol, describing it as a direct excitant of the respiratory centre whose action is not impaired by enervation of the carotid sinus (*Zunz*). (Particulars concerning the treatment of asphyctic states will be found in the sections dealing with Poisonings, Incidents during Narcosis, First-Aid and Pediatrics.) It is worth adding that *Jánossy* and *Palcsó* recommend also intracisternal Cardiazol injections in sudden paralysis of the medulla oblongata.

Krehl mentions that, in *cardiac dyspnœa*, Cardiazol is of assistance owing to its excitant effect on the respiratory and vascular centres. The remedy is recommended in the treatment of cardiac dyspnœa also by *Bohnenkamp*.

In cardiac debility as a sequel to *pulmonary emphysema*, *Bacmeister* places Cardiazol on the list of suitable remedies.

(d) Pneumonia, bronchopneumonia

According to *Naurratil*, *Lange* and others, Cardiazol is particularly valuable in the graver forms of pneumonia on account of its prompt *influence on the circulatory and respiratory centres*. *Hemmerling* praises the excellent effects of Cardiazol (subcutaneously or intravenously) in genuine pneumonia, stating that the vasomotor tonus is raised, the superficial respiration deepened and *expectoration facilitated*. Above all, he stresses the beneficial action on the nervous system.

Cardiazol is, among other remedies, recommended by *Curschmann* for the *care of the circulation in croupous pneumonia. Meinhard* also takes the view that Cardiazol is of much value in pneumonia for the support of the patients' natural strength, more especially that of the heart. *Schlesinger* reports particularly good effects with Cardiazol in *senile pneumonia* with declining heart power (10 drops, 3–6 times daily, or injections as required). For the treatment of acute pneumonia with genuine cardiac insufficiency, *Krehl* recommends digitalis, or strophanthin in combination with Cardiazol. *P. Krause* gives the preference to Cardiazol in acute circulatory debility as it appears to be especially effective at the commencement of respiratory disturbances. *Seyderhelm* describes the vasotonic properties of Cardiazol in pneumonia. *H. Scherf* gives Cardiazol, etc., to every pneumonia patient from the first day. According to *Raabe*, Cardiazol renders excellent services in preventing collapse in pneumonia (1 c.c., 2–4 times, subcutaneously). *Thannhauser* advocates early administration of cardiacs in *bronchiolitis:* Cardiazol and camphor for young persons; digitalis, in addition, for older people. In pneumonia cases where the circulation is seriously endangered, he gives injections of 1 c.c. Cardiazol every 2 hours. For the control of the circulation, Cardiazol and similar preparations are regarded as the remedies of choice by *Kleewitz. Bansi, Kalinke* and *Rohrlich* state that intravenous and intramuscular injections of 2 c.c. Cardiazol as a rule raise the oxyhæmoglobin content of the vein considerably after 10–40 minutes in pneumonia and other infectious disorders. The rise in the venous O_2 value is mainly due to an increase in the circulatory minute volume.

Sajdák recommends Cardiazol also as an *expectorant* in

croupous pneumonia. After an injection the pulse grows regular and strong, the general condition often improves strikingly, both objectively and subjectively. For continuous medication, the author uses Cardiazol liquidum and the tablets. *Schoenfeldt* regards Cardiazol as particularly indicated for the treatment of pneumonia in view of its powerful excitant action on the respiratory centre and its marked expectorant properties. *Esser* also stresses the favourable influence on expectoration. *Januschke* is another writer mentioning that Cardiazol promotes the ejection of infectious secretion and exudate from the bronchia and lungs. The favourable influence of Cardiazol in these cases is complemented by its proved stimulant action on the respiratory centre.

In grave cases of *bronchopneumonia*, analeptics such as Cardiazol are described as indispensable by *Bacmeister* who recommends Cardiazol, amongst other products, also in acute cardiac debility.

(e) Pulmonary tuberculosis

Amongst circulatory tonics in the treatment of tuberculosis of the lung, *Poindecker* gives prominence to Cardiazol. *Sattler* also prefers Cardiazol in the therapy of *chronic circulatory disturbances. v. Hayek* was able to effect improvement in the dyspnœa and feeling of exhaustion in grave tuberculous destructive processes with a toxically damaged heart, cyanotic tendency and grave dyspnœic conditions, by the administration of 10 drops Cardiazol liquidum daily during several weeks. Similar observations are reported by *Kozma* who also refers to the expectorant action of Cardiazol, stressing the fact that patients feel much better after this medication; their appetite improves so that a roborant therapy can be

instituted. It is also pointed out by *Altmann* that the continuous administration of Cardiazol in grave cases of pulmonary tuberculosis gives good results inasmuch as it raises the subjective condition and exerts a favourable influence on temperature and expectoration. According to *Bernstein*, Cardiazol raises the blood-pressure and thereby indirectly influences also the heart function. In addition, he mentions the action on the respiratory centre. Pulse irregularity and the symptoms of hypotension are gradually abolished by Cardiazol whilst the general condition improves. According to *K. Weiss*, pulmonary tuberculosis is a special indication for Cardiazol on account of its simultaneous effect on respiration and circulation. In pulmonary dyspnœa, the remedy was given in series: 1 to, at most, 2 ampoules, subcutaneously, every day for about 10–14 days. With this treatment the dyspnœic states disappeared with almost unbroken regularity or were, at any rate, much improved. Where myocardial decompensation existed, a combined digitalis + Cardiazol therapy was found to give the best results.

In cases of *secondary emphysema* and cardiac debility, Cardiazol (among other remedies) is used by *Dietlen*.

Bernstein has always observed a favourable action of Cardiazol in *hæmoptysis* due to congestion in the pulmonary circulation. On the first day of the bleeding he gives 1 ampoule subcutaneously every 2–3 hours, and on the following days 20 drops 3–4 times daily per os. *Heumann* recommends the injection of camphor preparations, or 1–2 ampoules Cardiazol, in hæmoptysis with an unsatisfactory pulse and impeded expectoration. *Mut y Gil* gives Cardiazol against hæmoptysis in combination with strophanthin. *Lindt* and other writers inject 1–2 c.c. Cardiazol

20 minutes after the administration of Clauden* in that disorder. *Unverricht* likewise combines blood-coagulants with subcutaneous Cardiazol injections in the treatment of pulmonary hæmorrhages.

The use of excitants (including Cardiazol) in manifestations of collapse after *spontaneous pneumothorax* is advised by *Bacmeister. Schlesinger* also advocates Cardiazol as an analeptic in cardiac debility following pneumothorax.

Pulmonary surgery: In *collapse treatment, Popper* and *Veber* used Cardiazol amongst other remedies against the respiratory disturbances following gas inflation. *K. Weiss* states that he has nearly always found a mixed syringe of 1 c.c. Cardiazol and 0·005 gm. morphine, given subcutaneously before inflation, to arrest the tachycardia and dyspnœa which occasionally arise in the course of pneumothorax treatment. The shock-like states of collapse occasionally experienced during artificial pneumothorax are also quickly remedied by Cardiazol which promotes a quick return to regular cardiac and respiratory activity. Cardiazol + morphine has also been found very useful in spontaneous pneumothorax with mediastinal displacement. After *phrenic evulsion*, the discomforts occurring during the first few days and due to a raised diaphragm, have been much relieved by Cardiazol + tinct. valerian. *Bernstein* also refers to the good services rendered by Cardiazol in pulmonary operations (*thoracoplasty*).

(f) Pulmonary embolism

In pulmonary embolism, *Goldscheider* uses, among other preparations, Cardiazol or, in certain cases, Cardiazol-Dicodid, to combat the cardiac debility, and *Bacmeister* also advocates the use of Cardiazol, etc., in such cases.

(g) Pulmonary œdema, pulmonary congestion

Cardiazol is, among other remedies, mentioned by *Krehl*, *Thannhauser*, *Bacmeister* and others, in connection with *pulmonary œdema*. *David* recommends intravenous injections of 0·5 mgm. strophanthin and 1 c.c. Cardiazol in 20 c.c. of a 20–40% glucose solution. *v. Breza* mentions a case of pulmonary œdema successfully treated with Cardiazol. Within a few minutes after the intravenous injection of 1 c.c., the alleviation was considerable; respiration grew calmer and deeper, the tracheal râles ceased gradually and cyanosis diminished to some extent. Patient had a quiet night. He received continuous doses of Cardiazol. With energetic Cardiazol treatment, the pulmonary œdema was repeatedly combated with much success; the patient's general condition, however, finally grew so much worse that therapeutic measures no longer availed. *Viessmann* has also had experience of the life-saving effects of Cardiazol in a case of pulmonary œdema. His patient was a woman of 50 suffering from nephrosclerosis and marked hypertension. Pulmonary œdema developed to an alarming extent following some physical exertion. The condition was so threatening that death seemed to be a question of minutes. Patient was at first given $1^1/_2$ c.c. Cardiazol intravenously. Respiration which had previously completely stopped deepened soon after the injection. The pulse improved considerably; consciousness returned. For the sake of ensuring the success, a further $1^1/_2$ c.c. Cardiazol was injected intramuscularly. The result is especially convincing if it is considered that the patient left her bed on the following day, contrary to the advice of her physician. *Knipping* is in favour of camphor and Cardiazol during the intervals of strophanthin therapy of pulmonary œdema: in desperate cases, Cardiazol intra-

venously, and camphor, if required, in large doses. *Braun* advises caution with morphine preparations in threatening pulmonary œdema but says that camphor preparations and Cardiazol can occasionally, and with due circumspection, be combined with codeine. *Durán Arrom* begins the treatment of pulmonary œdema with venesection and subsequently injects glucose solution plus Cardiazol, intravenously. *Fahrenkamp* also recommends venesection, large doses of Cardiazol, Dilaudid (Knoll), etc., in pulmonary œdema treatment.

Schoen remarks that vasomotor and respiratory stimulants with a central point of attack, e.g., Cardiazol, frequently display a favourable action in congestion of the lungs. *Kroetz* is of opinion that Cardiazol and similar substances are more to the purpose in *pulmonary congestion* than adrenaline or ephedrine.

(h) Pleuritis

According to *Grozdanović*, Cardiazol is valuable during the performance of *thoracic punctures*. The remedy is also given by *Thannhauser* against minor states of debility arising during the removal of the exudate.

C. Infectious Diseases

(a) General

In *circulatory debility* following any kind of acute infection, the early administration of Cardiazol and similar preparations is recommended by *Krehl*. Digitalis preparations are not likely to be of much use in acute infectious disorders of the heart-muscle, whereas Cardiazol, etc., may be expected to supply the maximum assistance. This opinion is shared by *Siebeck* who gives the preference to

Cardiazol in acute infectious disorders for the support of heart and circulation, this preparation being quicker in its action and having a simultaneous effect also on the respiratory centre. *Löhr* regards the circulatory analeptics (Cardiazol, etc.) as valuable adjuvants in the treatment of circulatory debility, more especially in infectious diseases of all kinds. Where indications permit he uses them even in circulatory failure due to primary cardiac insufficiency. Cardiazol is especially suitable because it is rapidly absorbed when given subcutaneously or intramuscularly and because the injections can be performed by any hospital nurse.

B. Kraus has used Cardiazol in acute myocarditis and endocarditis (in typhoid fever, influenza, scarlatina and acute infectious icterus); also as a *prophylactic* of cardiac involvement in the course of infectious diseases (the report refers to 250 cases of influenza and measles associated with bronchopneumonia).

The chapter on *Pediatrics* contains exhaustive details concerning the use of Cardiazol in *whooping cough, diphtheria, scarlatina, measles* and other typical, infantile infectious diseases.

(b) Typhus abdominalis (and paratyphus)

Štancl describes the effects of Cardiazol in 5 cases of subacute *arterial hypotension* in convalescents, also in one case of subacute arterial hypotension in a convalescent woman during a febrile relapse, and, finally, two cases of acute hypotension during the pyrexia stage. The action of Cardiazol was, i.a., seen in its influence on respiration which slowed and deepened. The heart frequency at the same time returned to normal. *Reig Cerdá* regards Cardiazol as a particularly suitable circulatory tonic in typhoid fever. Long-continued use produces no cumulation; the rapid and certain action normal-

izes the blood-pressure (increase of maximal, decrease of minimal pressure). According to *Fahrenkamp*, energetic analeptics (e.g., large doses of Cardiazol) will often have life-saving effects in typhus abdominalis with sudden collapse and signs of genuine vascular debility. *Denkoff* advocates the administration of Cardiazol and Digipuratum (Knoll) to all typhoid fever patients from the very beginning. *Winer-Bezbergowa* and *Penson* gave Cardiazol in 54 cases of typhoid fever. They remark on the improvement of pulse, blood-pressure and respiration whilst the medication lasts. The remedy was given per os in all cases, the majority of the patients receiving also subcutaneous injections of 2 c.c. every 3 hours. It was found that Cardiazol is especially useful in infectious diseases as an excitant of the circulatory and respiratory functions. *Serafinski* gave Cardiazol to about 25 patients suffering from epidemic abdominal typhus. He injected 1 c.c. Cardiazol thrice daily, or else gave the medicament per os. Improvement of the circulatory function was observed in every case. *Hemmerling* finds that, in typhoid fever, Cardiazol abolishes the apathetic state and revives the patients' interest in their environment.

Cardiazol figures amongst the remedies recommended by *Friedemann* in *paratyphus*.

(c) Psittacosis

Hegler gives Cardiazol against the circulatory debility engendered by parrot disease.

(d) Sepsis

In *Leschke*'s opinion, the treatment of circulatory debility in sepsis must, above all, take into account the danger of vasomotor

paralysis: vascular remedies, e.g., Cardiazol, are indicated in the first place. *Franck* mentions Cardiazol among the remedies indicated in failing cardiac power. *Esser* and *Schoenfeldt* also publish their favourable experiences with Cardiazol in sepsis.

(e) Plague

In pneumonic plague, *Schutt* uses (i.a.) Cardiazol as an adjuvant in Omnadin* treatment.

(f) Malaria

According to *Weselko*, the results given by Cardiazol — either alone or in combination with other medicaments — are so satisfactory that the remedy may be regarded as indispensable in modern malaria treatment, especially in malarial cachexia (vomiting). His clinical experience shows that Cardiazol has not only a restorative and tonicizing effect, but it is also stated to possess antitoxic properties, which latter appear to have a distinctive power against the malarial toxins. In a case of tonic-clonic spasms and deep unconsciousness in a 7-year-old malaria-infected girl, the spasms ceased for 1/2 hour 8 minutes after the injection of 1 c.c. Cardiazol. A further injection of 1 c.c. Cardiazol brought the child round completely after 1 hour. In the further course of the treatment *Weselko* used a combination of quinine mur. 0·3 gm., Cardiazol 0·05 gm. ad capsul. amyl. (1 capsule, 3 times daily, 1/2 hour after meals). Cardiazol is also recommended by *Muhlens* in malaria.

Hegler advocates (i.a.) Cardiazol in the treatment of circulatory debility in *blackwater fever*.

(g) Ague

According to *Breitbarth* and *Habernoll*, brilliant results have been obtained from Cardiazol in ague where it combats the serious decline in vascular tone (which, in one case, led to collapse).

(h) Infectious pharyngeal catarrh

v. d. Velden says that Cardiazol renders good services in the treatment of residuary manifestations of protracted infectious pharyngeal catarrhs in elderly people.

(i) Angina

Among other authors, *Parfanowicz* and *Schoenfeldt* describe the good results attainable with Cardiazol in angina.

(k) Influenza

Moewes finds that, in influenza and other acute infectious diseases, Cardiazol deepens respiration and facilitates expectoration, apart from its beneficial action on the circulation. *Freund* is in favour of the use of Cardiazol for early specific circulatory therapy (occasionally in combination with ephedrine). For the protection of heart and circulation in influenza, *Ortner* recommends substitution of digitalis by caffeine or Cardiazol.

Licci has tried Cardiazol in acute cardiac debility, especially that occurring in *influenzal pneumonia*. *Pochmann* reports that many lives were saved during an influenza epidemic by subcutaneous and intravenous Cardiazol injections (repeated at intervals of $^1/_2$–2 hours, according to the severity of cases), the patients being chiefly elderly people afflicted also with complicating bronchopneumonias *and loss of resistance. The action of the Cardiazol injections* manifested itself remarkably quickly; the radial

pulse grew fuller, respiration slower and deeper, existing cyanosis diminished gradually and the subjective condition improved. *Serafinski* has used Cardiazol in a series of cases of influenzal pneumonia and states that improvement followed in every case (retardation and increased tension of the pulse). *Eimer* and *Kestermann* give the preference to Cardiazol (i.a.) for the treatment of the circulation in influenzal bronchopneumonia, and excellent results have been achieved with the remedy by *Pascarelli* in influenza, pneumonia and bronchopneumonia, both as regards the general condition and the state of the pulse which improved considerably; respiratory frequency lessened and breathing became deeper.

(l) Tetanus

In tetanus, *Buzello* gives injections of camphor or Cardiazol from the very first day. Among the remedies indicated against circulatory debility in *serum disease* (tetanus serum), *Baumann* recommends Cardiazol.

(m) Dysentery

In dysentery, *Hegler*[1] attributes importance to early measures against circulatory debility and, amongst other remedies, mentions Cardiazol. *Franck* also favours treatment with Cardiazol, etc. *Schlesinger* supports the heart action from the first, mentioning Cardiazol among the remedies valuable for that purpose.

(n) Amœbiasis

Basile recommends a combination of Cardiazol or similar restoratives with emetine in the treatment of amœbiasis in view of the possible development of cardiac and circulatory debility.

(o) Cholera (asiatica)

Hartleben and *Schad* recommend adequate support of the circulation in cholera asiatica, more especially by means of vascular remedies (i.a. Cardiazol). *Hegler*[2] suggests the addition of adrenaline or Cardiazol to the physiological salt infusions.

(p) Erysipelas

Turyn describes the favourable action of Cardiazol in erysipelas. *Hegler*[1] gives 15 drops of Cardiazol, thrice daily, in cardiac disturbances, irregularity or softness of the pulse. *Volk* also recommends Cardiazol as one of the circulatory tonics to be used in erysipelas. Immediate support of the circulation, e.g., by Cardiazol, in erysipelas, is also advocated by *Hayward. Scherber* invariably uses Cardiazol and Digipuratum (Knoll) in erysipelas for the same purpose.

(q) Articular rheumatism

Hegler[3] mentions Cardiazol as one of the remedies given by him against cardiac debility. *Franck* treats rheumatism by intravenous injections of Sanarthrit* and Cardiazol (in the mixed syringe).

Janson, writing on the treatment of obstinate rheumatic polyarthritis, advocates the use of the following prescription: Atophan sodium* 5·0, Cardiazol (10%) 5·0, Melubrin* 10·0, sodium salicyl. 15·0, aqua dest. ad 100·0 gm. Of this (lukewarm) mixture, he injects 10 c.c. at a slow rate, intravenously (for 3–6 days).

(r) Dengue

Against vasomotor debility, *Floros* administered Cardiazol (amongst other remedies).

(s) Typhus exanthematicus (Spotted Fever)

Israel speaks of his favourable experience with Cardiazol in various infectious diseases, including exanthematic fever. Cardiac debility should, according to *Franck*, be treated with Cardiazol, etc.

(t) Weil's disease (Icterus infectiosus)

Hegler advocates immediate measures, e.g., administration of Cardiazol, in vasomotor collapse due to infectious icterus. *B. Kraus* also relates his favourable experience with Cardiazol in the same disorder.

Addenda

Serum shock and anaphylactic shock

Serum shock can, according to *Krehl*, generally be overcome by adrenaline and Cardiazol. In serum shock, *Buzello* advises immediate interruption of the serum injection and intravenous administration of 2 c.c. Cardiazol. In *Gierthmuhlen*'s view, conditions of shock following serum injections demand support of the circulation above everything. Among substances valuable for that purpose he mentions Cardiazol. *Mihailovici* also uses Cardiazol in the treatment of serum disease. *Kämmerer* recommends analeptics of rapid action, e.g., Cardiazol, in anaphylactic shock (serum disease) with collapse. *Herholz* administered Cardiazol (i.a.) in a case of anaphylactic shock resulting from non-specific stimulation therapy and Cardiazol is among the remedies used by *Schott* in cases of serious shock. According to *Hartleben* and *Schad*, Cardiazol, etc., are suitable also for the prevention of serum shock.

Intracutaneous skin tests

Carrié suggests the desirability of Cardiazol and adrenaline injections always being kept at hand for the treatment of shock-like manifestations resulting from intracutaneous skin tests.

Post-vaccinal encephalitis

Pereira and *Oliveira* are in favour of administering Cardiazol, partly per os, partly by injection, during the entire course of the affection.

D. Poisoning

(a) General

In poisoning by hypnotics, opiates, alcohol, nicotine, decomposed food, vegetable and animal toxins (poisonous mushrooms, snake-bite), the use of analeptics with a central attack has proved extremely valuable to combat circulatory and respiratory insufficiency. Cardiazol has, in this connection, the additional advantage of combining the properties of a respiratory stimulant with those of a circulatory tonic, of being perfectly tolerated and involving no risk of overdosage even though given at short intervals. According to *Behrend*, the dose generally necessary in serious poisoning by hypnotics, etc., is 5–10 c.c. of a 10% Cardiazol solution, injected partly intravenously and partly intramuscularly.

Schoen says that narcotic poisoning is the domain of Cardiazol (etc.). Many instances are cited in the literature in which the purposeful application of these remedies has saved life, contrary to expectation. The beginning, peak and subsidence of the therapeutic action can be followed in the patients in a manner analogous to experiment. The most impressive points are improve-

ment in respiration and pulse and the measurable increase in the blood-pressure. In addition, we witness recovery of the sensorium, increased tonus of the musculature, improved reflex action, outbreak of perspiration, which, with high dosage, indicate the optimal centrally excitant effect and the nearness of the convulsive threshold. According to *Balázs*, the incidence of disturbances of the vasomotor centre and vascular periphery in acute poisonings very frequently plays an important role. In these cases the administration of digitalis is of little assistance, whereas caffeine, strychnine, adrenaline, Cardiazol, and especially Cardiazol-Ephedrine with its rapid and enduring action, are more likely to be helpful.

(b) Poisoning by carbon monoxide, domestic gas, etc.

Wirth and *Muntsch* recommend Cardiazol and other medicaments in cases of *carbon monoxide poisoning*. *Teleky*[1] gives subcutaneous injection of Cardiazol, etc., in these cases for the purpose of resuscitation. According to *Trendelenburg*, the stimulant action of Cardiazol on respiration renders it particularly indicated in carbon monoxide poisoning. *Krehl* is another writer advocating the use of Cardiazol in this connection. *Kötzing* describes the treatment of 42 cases of carbon monoxide poisoning and 9 cases of *sulphuretted hydrogen poisoning* by hourly repeated subcutaneous injections of 1 c.c. Cardiazol to support respiration and circulation. The result was a long enduring, uniformly excitant, action on the centres. Intravenous injections were only given in cases of extreme urgency. Good results with Cardiazol in poisoning by carbon monoxide and carbonic acid are reported also by *Turyn*.

Pochmann gives Cardiazol by intravenous injections with much success in acute poisoning, more particularly from carbon monoxide and *domestic gas*. *Rajna* says that Cardiazol is particularly valuable in poisoning by domestic gas, carbon monoxide, etc. *Schwab* has given Cardiazol in more than 30 cases of domestic gas poisoning, in continuous subcutaneous and intramuscular doses (in combination with oxygen). The remedy was always well tolerated and never failed in its action. *Dubois-André* records his excellent results with Cardiazol in poisoning by domestic gas. *Hippe* writes that consciousness is quickly regained where Cardiazol is given in cases of domestic gas poisoning. In the same connection, Cardiazol is recommended by *Pal*, *Teleky*[2], and others.

Zangger advocates *immediate intracardial injection of Cardiazol*, etc., in cases of unconsciousness due to the *inhalation of motor car exhaust-gases* (in garages).

(In these cases, repeated injections of 1 c.c. Cardiazol are preferable to the administration of a large amount in one dose.)

(c) Alcoholic poisoning

Phillips and *Kese* (i.a.) report good results from Cardiazol in alcoholic poisoning. The remedy stimulates circulation and respiration and favours elimination of the poison. Also *Fuhner* speaks of Cardiazol as a stimulant of the respiratory centre in alcoholic poisoning. *L. Kraus* effected considerable improvement in *the alarming symptoms (failing heart and pulse, difficult respiration)* following serious alcoholic poisoning, by injections of Cardiazol (after stomach lavage). *Dietrich* mentions that 1–2 Cardiazol tablets (taken in a peppermint infusion) have a surprisingly power-

ful restorative effect, especially in the slighter forms of alcoholic poisoning. The distressing symptoms such as malaise, retching, cerebral numbness, headaches, psychic depression, etc., disappeared in the majority of the cases observed.

(d) Poisoning by morphine preparations

Hemmerling reports that Cardiazol (1 c.c., twice, subcutaneously) after morphine poisoning restores the patients' consciousness very speedily. *Jost* describes the case of a 73-year-old woman with unmistakable signs of morphine poisoning. He injected the patient with 2 c.c. Cardiazol intravenously in the space of 2 minutes, with the result of an immediate analeptic effect. Another injection of 1 c.c. Cardiazol was given $^1/_2$ hour later. Respiration then returned to normal and the hitherto numbed sensorium cleared up quickly. This represents a case of a moribund, scarcely breathing patient being restored to normal physiological conditions by 3 c.c. Cardiazol administered in the space of about $^1/_2$ hour. *Dubois-André*, *Rajna* and *Turyn* have also achieved very good results with Cardiazol in morphine poisoning. *Bruns* and *Thiel* employ even intracardial injections, e.g., of Cardiazol, in serious cases of narcotic poisoning. *Jánossy* advocates intracisternal Cardiazol injections in poisoning by narcotics (morphine) or carbon monoxide.

Vera speaks of the extremely valuable services rendered by Cardiazol in the abolition of ill-effects on the heart in chronic intoxication produced by morphine-scopolamine. In chronic poisoning by opium derivatives, with myocarditis as a sequel, oral Cardiazol medication enabled systematic *withdrawal cures* even in seriously debilitated patients. Also in acute poisoning,

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with remarkable promptness; the patient, a pregnant woman, 34 years of age, had taken 15 tablets of an analgesic. She was discovered in an apathetic state, exhibiting extreme pallor, practically collapsed, and moaning. She was given 5 c.c. Cardiazol intravenously and 5 c.c. intramuscularly; the effect was rapid, the patient being clear in her mind after 20 minutes. Stomach lavage was dispensed with because the preparation had been taken several hours previously; the success is, therefore, clearly ascribable to the action of the Cardiazol alone. *Nick* records another instance of life saved by Cardiazol in grave hypnotic poisoning; he gave an intravenous injection of 5 c.c. Cardiazol in one dose and another 5 c.c. by the intramuscular route. Already after 10 minutes there was considerable improvement. In the course of the next hour 10 more ampoules were injected, partly intravenously, partly subcutaneously. *Greve* saw a similar case: that of a woman who had taken 21 tablets of a barbituric acid preparation within 15 hours; her speech was paralyzed; she suffered from herpes labialis and incontinentia urinae. Here Cardiazol was as successful as in the cases previously related. *O. L. Weiss* says that, in barbituric acid poisoning, Cardiazol is superior to all other restoratives. *Phillips*, *Rajna*, *Dubois-André* and others also discuss the successful results achieved by Cardiazol in hypnotic poisoning.

(f) Poisoning by putrid food (including mushroom poisoning)

Biedermann has had good results with Cardiazol in serious cases of *meat poisoning*. *Rosner* and *Kornblueh* publish their equally favourable experiences with Cardiazol treatment of poisoning by putrid food. *Slauck* has used the remedy with advantage in botulism.

Cardiazol very rapidly abolishes the semi-comatose condition and there is no risk of secondary manifestations such as seen after caffeine.

(e) Hypnotic poisoning (particularly by barbiturates)

Leschke, *Morawitz* and others name Cardiazol among the substances indicated for the treatment of *acute hypnotic poisoning*. *Pick* holds the view that preparations (like Cardiazol, etc.) whose action is not restricted to the cerebral cortex, are particularly useful in hypnotic poisoning. *Pohlisch* and *Panse* speak of good results from Cardiazol, etc., as circulatory tonics in serious cases of hypnotic poisoning.

One of the latter is described by *Deglmann*. Stomach lavage was immediately performed and 5 c.c. Cardiazol injected intravenously and 5 c.c. intramuscularly at the same time. Another 5 c.c. was given intravenously after 3 hours, followed by 3 c.c. intramuscularly at intervals of 2 hours. In this manner the patient, a woman, received 35 c.c. Cardiazol in the course of a single night. Although she did not wake up, respiration became normal and the heart action improved; the danger of pulmonary œdema was no longer present. Reflex action to powerful stimuli returned only by the end of the following day, during which liberal doses of Cardiazol had been given. The general condition had then so far improved that there was no further danger to life; consciousness returned 43 hours after admission. An immediate rousing effect was not to be expected in view of the grave nature of the case, but life was saved by the maintenance of the patient's vital functions. *Spiegel* also publishes a case of serious barbituric acid poisoning. In this instance the rousing effect of Cardiazol ensued

other cases, the insects had attacked particularly sensitive parts of the organism (tongue, upper lip, genitals). In addition to violent pains the parts were much swollen. In one case the swelling of the tongue appeared to render tracheotomy unavoidable but injections of calcium and Cardiazol saved operation and were followed by curative results also in the rest of the cases.

(l) *Other kinds of poisoning*

Ethyl chloride

Wellisch describes the case of a man, aet. 33, who tried to commit suicide by drinking nearly 80 gm. ethyl chloride. The author saw him 7 minutes later, washed out his stomach and treated him with camphorated oil and caffeine. Despite these measures the patient grew worse, with muscular twitching, impalpable pulse and a completely asphyctic state. A single subcutaneous injection of Cardiazol (1 c.c.) effected remarkable improvement; the pulse grew full, respiration was restarted and all danger removed in $1^1/_2$ hours during which some further injections of $^1/_2$ ampoules of Cardiazol were given.

Aniline, chloraniline, nitrobenzol

Kotzing gave hourly subcutaneous injections of 1 Cardiazol ampoule until respiration and circulation were restored. *López Pondal*, describing a case of aniline poisoning in a child of 13, mentions that among other remedies he also used Cardiazol.

Arsenic

Beutel had a case of arsenious acid poisoning, successfully treated with Cardiazol. *Hegler* also includes Cardiazol among the

Leschke[1], *Morawitz* and others recommend Cardiazol against the circulatory debility resulting from *mushroom poisoning. Nissen* began his treatment of a case of morel poisoning with circulatory *tonics, including also Cardiazol. Steinbrink* and *Münch* are not in favour of camphor in agaricus poisoning, because its detoxication does not appear assured in view of the ensuing hepatic disturbance. Cardiazol figures among the circulatory remedies recommended by these authors in the place of camphor. *Welsmann* advocates the administration of more than the customary doses of Cardiazol in mushroom-poisoning, especially by agaricus phalloides, so as to effect improvement by the energetic excitation of the vasomotor centre. The simultaneous stimulating effect of Cardiazol on respiration also appears to play an important part here.

(g) Snake-bite poisoning

Becmann has treated a number of cases of snake-bite with intravenous injections of 1 c.c. Cardiazol (and Cardiazol-Ephedrine). Cardiazol is also among the remedies recommended by *Morawitz* and *Leschke*[2] for the treatment of the bites of poisonous snakes (vipers) on account of its restorative properties. *Werwath* administers Cardiazol, etc., in collapse following viper-bites.

(h) Poisoning by insect-bites

Janson advocates the use of Cardiazol as a prophylactic of respiratory and circulatory disturbances in serious insect-bite. In one of his cases an exceptional number of bee-stings led to serious respiratory and circulatory trouble. All danger was quickly abolished by an injection of Cardiazol (2 c.c. intravenously). In

Cocaine

Bücking had a case of cocaine poisoning in which he administered copious doses of Cardiazol.

Digitalis

Cardiazol has been found of great value in cases of acute digitalis poisoning, as reported by *B. A. Schwartz*. *Moravitz* also includes Cardiazol among the remedies to be given in serious cases of digitalis poisoning.

Salts of lemon (potassium acid oxalate)

Gies and *Polstorff* state that they have administered circulatory remedies such as Cardiazol in poisoning by salts of lemon.

Lysol

Beutel publishes a case of lysol poisoning successfully treated by Cardiazol. *Burg* used the remedy in the case of a lysol-poisoned person suffering from bilateral, central pneumonia (46 intramuscular injections in all).

Nicotine

Schoenfeldt advocates the use of Cardiazol in nicotine poisoning. *Leschke* likewise gives Cardiazol in the treatment of serious nicotine poisoning. According to *Hofstätter*, Cardiazol is a good palliative of the milder abstinence symptoms in cases of tobacco withdrawal.

Nitrous Gases

In poisoning by nitric acid vapours, *Laun* recommends, apart from immobilization, warmth and oxygen administration (with-

remedies able to revive patients after collapse in acute arsenical poisoning.

Barium

Cardiazol is included in the remedies used by *David* against poisoning by barium.

Hydrocyanic acid

In hydrocyanic acid poisoning, *Enger* gives Cardiazol (among other remedies) for the stimulation of respiration and circulation. *Kayser* uses injections of lobeline and Cardiazol. Among antidotes in hydrocyanic acid poisoning, Cardiazol is also mentioned by *Novellas Roig.*

Cantharides ointment

In poisoning following the use of cantharides ointment, *Wysocki* gives injections of Cardiazol, or Cardiazol tablets, during the first days of treatment and in adequate dosage.

Carbonyls (especially nickel carbonyl)

Kötzing had 13 cases of nickel carbonyl poisoning and relates that the symptoms of irritation of the respiratory passages and circulatory disturbances were abolished in a few days by inhalation of a 1% Normosal* solution and 4 subcutaneous injections of Cardiazol daily. Injections of Cardiazol (1 c.c.) or digitalis are recommended also by *Amor* for the treatment of cardiac debility following nickel carbonyl poisoning. *Koelsch* gives Cardiazol, etc., in circulatory debility due to carbonyl poisoning.

8 ammonia) in which he gave Cardiazol subcutaneously to provoke a better and quicker blood perfusion of the affected organs. Apart from the effect on the circulation, the influence of Cardiazol on the respiratory centre was conspicuous. In connection with nitrous gases and phosgene poisoning, the method of treatment as described resulted in the impression that the risk of pulmonary œdema was lessened.

(Where damage results from the inhalation of any other irritant substances, Cardiazol is indicated for the prophylactic support of the circulation, quite apart from its remedial value in actual lung damage.)

Sulphur dioxide

Kötzing treats cases of acute sulphur dioxide poisoning with Cardiazol, etc.

Carbon tetrachloride

Henggeler had a serious case of carbon tetrachloride poisoning. On the 22nd day of the illness, the state of the patient had so seriously deteriorated that the pulse began to fail and death appeared certain. As a last resort, Cardiazol was injected, 1 ampoule every four hours. The result was striking. The patient, who through constant vomiting had lost fully 43 lbs, vomited only 4 times on the second day; on the fifth day, singultus and retching had disappeared so that oral feeding could be resumed without interruption; patient then received nourishing food and 1 Cardiazol tablet, 3 times daily. His recovery made good progress and after a few weeks patient weighed 3 lbs more than his original weight.

out pressure), that the attendant should, in the presence of alarming symptoms (debility, thoracic oppression, dyspnœa) if possible give a subcutaneous Cardiazol injection (1 ampoule), so that the doctor may perform venesection, followed by a glucose injection, as soon as he arrives. *Muntsch* also advocates Cardiazol injections in poisoning from nitrous gases.

Phosgene

According to *Büscher* and *Muntsch*, the pulmonary œdema and its sequels which dominate the entire picture in phosgene-poisoning are indications for venesection, for injections of strophanthin, Digipuratum (Knoll), and, in addition, 1 c.c. injections of Cardiazol (repeated if necessary) for the tonicisation of the circulation and the highly important maintenance of the excitability of the respiratory centre. Cardiazol is among the remedies recommended for use in phosgene-poisoning also by *Berlet*, *Bohnenkamp*, *Dautrebande*, *Gillert* and others.

Phosphorus

Polak Daniels gives Cardiazol, etc., as a circulatory tonic in acute phosphorus poisoning.

Mercury

Hug and *Sanguinetti* use hypertonic grape sugar solution, intravenously, combined with Cardiazol, by way of complementary treatment in mercury poisoning.

Irritant gases

Kötzing had 37 cases of poisoning by irritant gases (5 nitrous gases, 3 phosgene, 5 sulphurous acid, 8 chlorine, 8 acid fumes,

Frerking, writing on narcotic withdrawal cures, favours large doses of calcium supported by Cardiazol, whereby states of physical exhaustion often undergo far-reaching improvement.

E. *Disorders of the Digestive Organs*

(a) Stomach and intestines

After serious hæmorrhages from *acute gastric ulcers and hæmatemesis* with a weak heart action as a sequel, *Franck* administers Cardiazol (among other remedies).

The same author advocates injections of Cardiazol, etc., in cardiac debility following *acute intestinal catarrh. Scharpff* advises the injection of strophanthin in 20 c.c. of a 20% glucose solution combined with Cardiazol in the same syringe in the treatment of acute intestinal catarrh (enterocolitis) where myocardial damage exists. This method succeeds in helping patients over the critical days where, in hypertension, the heart is (even on normal days) at the end of its capacity, or where patients suffer from a slight, or also serious, degeneration of the heart-muscle.

In *ulcerous colitis associated with anaphylactic shock*, the circulation requires careful watching and Cardiazol is one of the remedies to be administered if called for (*Franck*).

According to *v. Noorden*, a mixture of Cardiazol (0 1 gm.) and papaverine (0 04 gm.) has been found useful in *spastic constipation*.

For the treatment of *acute intestinal occlusion*, *Heusser* recommends the administration either of digitalis or circulatory tonics (Cardiazol, etc.), according to circumstances.

Franck includes Cardiazol among the remedies of benefit in

Thallium

Werner mentions a case of thallium poisoning in which Cardiazol was given against acute circulatory debility (apart from other remedies).

Trichlorethylene

Brednow and *Knorre* treated a case of trichlorethylene-poisoning with 0·002 gm. lobeline and 1 c.c. Cardiazol.

Worm powder

Brüning advocates the administration of excitants (Cardiazol, etc.) where indicated in manifestations of poisoning by worm powder.

Addendum

Withdrawal cures. (Morphine, etc.)

In cases of morphine withdrawal where the temperature rises above 38·5° C. during twilight sleep, *Potzl* recommends rousing patients by intravenous injections of 2 c.c. Cardiazol, 3–4 times daily. *P. Wolff* advocates the administration of circulatory remedies, including Cardiazol, in withdrawal cures for prophylactic purposes. *Schlomer* also uses Cardiazol (1 injection thrice daily), etc., prophylactically against respiratory disturbances during morphine withdrawal cures. According to *Görlitz*, the best results are obtainable from Cardiazol in its tablet form where the circulatory action declines during morphine withdrawals. *Vera* gives repeated doses of Cardiazol for several days before commencing any withdrawal cure. *Bieling* has used Cardiazol for the treatment of circulatory disturbances during an opiate withdrawal cure.

F. Diseases of the Urinary Organs

(vide also Urology)

Cardiazol is amongst the remedies used by *Straub* against cardiac insufficiency in *acute nephritis.* Also *Weltmann* is in favour of cardiac treatment with digitalis and Cardiazol in acute nephritis. *Fleckseder* gives, i.a., Cardiazol (preferably intravenously in a 20% glucose solution) in chronic bilateral kidney disease with high blood-pressure where decompensation threatens or is already conspicuously established.

In uræmia, *Franck* gives early injections of digitalis against cardiac debility, but starts, if possible, with an intravenous injection of $^1/_2$ mgm. strophanthin, combined with 1 ampoule of Cardiazol, etc. In *pseudo-urœmic states, Bauke* advises treatment of the cardiovascular apparatus with strophanthin, caffeine, Cardiazol, and purine derivatives.

According to *Grozdanovič*, Cardiazol (2 c.c. subcutaneously) has proved useful in *abdominal punctures* of debilitated persons or patients with copious exudates.

G. Metabolic Disorders

(a) Coma diabeticum

Cardiazol is amongst the remedies recommended by *Krehl, Escudero* and many other writers in diabetic coma in which state it is, according to *Franck*, of the utmost importance to strengthen the heart action by subcutaneous injections of camphor, Cardiazol, etc., every $^1/_2$–$^3/_4$ hour and, if necessary, with strophanthin in addition. *Kleeberg* gives intravenous injections of 2 c.c. Digipuratum (Knoll) + Cardiazol against the grave cardiac and cir-

cholera nostras associated with cardiac debility. *Kissling* advises the addition of analeptics such as Cardiazol to sodium chloride infusions given in summer diarrhœa if the pulse is unsatisfactory.

Veilchenblau speaks of good results from combined injections of 0·04 gm. Pantopon* and 2 c.c. Cardiazol in acute cholera nostras. He reports immediate improvement.

(b) Liver and bile-ducts

In acute *biliary colic*, *Reicher* recommends a combination of 0·0025 gm. Dilaudid (Knoll), 0·0005–0·001 gm. atropine sulphate and $^1/_2$–1 ampoule Cardiazol. The Cardiazol addition has proved especially valuable in the case of patients with a weak heart. In most cases the injections had a complete sedative effect after 15–20 minutes. Secondary effects were absent even in patients who had previously been unable to tolerate narcotics and who related that their reactions to the latter had always been fainting attacks and alarming cardiac collapse. *Kaiser* mentions a case of collapse during a painful attack of biliary colic in which Cardiazol was administered subcutaneously, improvement resulting after 4 minutes. *W. Wolff* advocates the simultaneous injection of morphine with camphor or Cardiazol in *cholecystopathies* in order to cancel out any possible unfavourable influence of the morphine on the circulation.

(c) Peritoneum

In acute *peritonitis* with cardiac insufficiency and premonitory signs of collapse, *Franck* administers Cardiazol, etc. Cardiazol is also recommended by *Stepp* against collapse in peritonitis.

The attacks grew less frequent, did not last longer than 20 minutes, generally ran a very mild course and did not recur oftener than once in 3–4 weeks. Pulse frequency fell from 140 to 95/100. As the case improved so was the Cardiazol dosage diminished.

(c) Addison's disease

The circulatory tonics of rapid action such as Cardiazol are recommended by *Thaddea* in the crisis (collapse) of Addison's disease, to be administered every 2–3 hours as long as the blood-pressure remains abnormally low.

H. The Medical Side of Sports. First-Aid Service.

I. Sports

(a) General

Overexertion, states of exhaustion, collapse, fainting, heat- and sunstroke

In their attendance on contestants in games, etc., *Rosner* and *Kornblueh* use Cardiazol against acute circulatory debility, shock and collapse due to *intensive effort*, as well as in cases of heatstroke, etc. They have also administered Cardiazol, in some instances in combination with quinine (Cardiazol-Quinine-dragées) in *grave states of exhaustion*, with excellent results. *Rajna* says that in *collapse* and serious cardiac debility, of frequent occurrence in prolonged and arduous contests, the damaged heart is quickly revived by Cardiazol. *Szèrmerowna* and *Reichert* regard Cardiazol as indicated for the treatment of many forms of physical exhaustion as the sequel of forced marches or hard-fought games. Seeing that incidents in sports are mainly attributable to vascular

culatory insufficiency. In this connection the excellent effect of Cardiazol has also been observed by *Hippe. v. Lebinsky* gave a subcutaneous Cardiazol injection to a comatose diabetic patient with the result that the previously impalpable pulse could be felt after 5 minutes and maintained its improved condition. Patient was given another injection of 1 c.c. Cardiazol intramuscularly after 1 hour. 24 hours later the pulse was relatively good, a success clearly due to the 2 Cardiazol injections. *Silva Telles* advocates, apart from insulin treatment, injections of Cardiazol, etc., the injections to be repeated at least every 2 hours. In threatening collapse they may be given intravenously. In the treatment of diabetic coma, the administration of circulatory tonics (apart from insulin) is recommended also by *Bertram* who, among other remedies, mentions Cardiazol, given subcutaneously in doses of 1–2 c.c.

In *hypoglycæmia*, *Reinwein* uses a 25% glucose solution with Cardiazol.

(b) Graves' disease (Basedow)

Against the feeble heart action in Graves' disease, *Rietti* gives Cardiazol (per os or subcutaneously). In very serious cases of Graves' disease with extreme tachycardia, emaciation, coma, etc., it is *Sturm*'s practice to give intravenous glucose infusions every hour, supporting the circulation at the same time by injections of Cardiazol or similar remedies, every $^1/_2$–1 hour. *Wolf* and *Sherwin* describe the case of a woman suffering from Graves' disease whose attacks persisted for more than an hour and were associated with pains and dyspnœa. 2 tablets of Cardiazol given after meals proved very beneficial whereas digitalis had no effect.

7200 metres, his condition being so grave as to arouse the greatest possible alarm. Cardiazol tablets, administered at regular intervals, not only enabled him to get through an especially difficult night at a height of 7000 metres, but to begin the descent on the following day in a relatively satisfactory state, managing even difficult situations. The initially very grave symptoms improved visibly and disappeared shortly after without the help of further medicinal treatment. On the strength of this experience, *Allwein* advocates the *inclusion of Cardiazol in the medical stores of all mountain shelters*, being convinced also that the transportation of mountain casualties to the valleys must be considerably facilitated where patients are supported by Cardiazol, and that it must be of great value in alpine accidents of various kinds, e.g., through avalanches. *Rajna* also speaks of the good effects of Cardiazol on *exhausted tourists and mountaineers* experiencing difficulties at high altitudes. *Calcaterra, Henggeler* and *A. Krause* praise the value of Cardiazol to mountaineers (in *mountain sickness*). *Apostol* makes his mountaineering patients take prophylactic doses of 10 drops Cardiazol, twice daily for 3 days, previous to their proceeding to high altitudes and, for curative purposes, gives 1 Cardiazol injection daily for 3 days. *Gut* recommends the remedy in tablet form in exhaustion and mountain sickness. According to *Zsigmondy-Paulcke*, Cardiazol is most valuable for reviving climbers after avalanche accidents when it is best given subcutaneously, which, in emergencies, can be done by any travelling companion.

O. Fischer gave small doses of Cardiazol with much success to persons with not entirely sound hearts, staying at *high altitudes in the tropics.*

and not to cardiac disturbances, *Majdrakoff* recommends the use of analeptics to support the circulation; in particular he mentions Cardiazol. The state of the circulation undergoes practically instantaneous improvement after an injection. With oral administration, the action develops within a few minutes. An important point is that the remedy is entirely innocuous. In further trials it was found that Cardiazol is able to increase physical output and to prevent circulatory disturbances arising from specially strenuous efforts. The favourable influence of Cardiazol was not only seen subjectively in a considerable improvement of the condition, but also objectively in the state of the pulse and blood-pressure. In complete circulatory failure, *Rautmann* restores his patients with analeptics such as Cardiazol.

According to *Schwarz*, Cardiazol proved of value also in *fainting attacks* and heatstroke, in the place of Hoffmann's Drops. *Lichtwitz* mentions Cardiazol among the remedies to be given in fainting attacks, etc. *Gallavardin* also makes use of Cardiazol injections in fainting fits.

Fantus gives Cardiazol, in 1 c.c. intravenous doses, in states of exhaustion due to heat. The suitability of Cardiazol in cases of *heatstroke* is also mentioned by *Bhattacharji*. *Wucherpfennig* recommends, among other measures, the injection of Cardiazol in *sunstroke* to support the circulation.

(b) Special cases

Mountaineering

Allwein has published his experience with Cardiazol during expeditions, especially at high altitudes. A member of the *1931 Himalaya expedition* collapsed after reaching an altitude of

II. First-Aid

(a) General

To restore consciousness, *Bruns* gives Cardiazol intravenously in doses of 1–5 c.c., the injections being performed at the slowest possible tempo and repeated several times if the condition requires it. The repetitions involve no risk. Intracardial injections of adrenaline in combination with Cardiazol, etc., may also be administered. *Hans* advocates injections, especially Cardiazol, etc., for revivification purposes. *Grossbauer* gives Cardiazol in shock and collapse following *accidents*, etc.; also in circulatory debility, *poisoning* by illuminating gas, carbon monoxide, spoiled food, *apparent drowning*, *exhaustion* due to overexertion in sports, and so forth. His rule is to give the remedy subcutaneously or by deep intramuscular injection. In emergencies he uses the intravenous, in slight cases, the oral route. 1 c.c. is the dose mostly administered by him; only very grave cases require the immediate application of 2 c.c., followed by the injection of 1 c.c.-doses at $^1/_2$–1-hourly intervals until all danger is removed. Important fields of indication for Cardiazol are, according to *Rajna*, – apart from cases of poisoning – shock and collapse due to contusions, *traffic accidents* and *burns*. *Lugones*[1] recommends the administration of cardiotonics, such as Cardiazol, etc., in *traumata* with syncope or collapse; furthermore, *Lugones*[2] uses Cardiazol in the treatment of *hæmorrhagia*. Very satisfactory results with Cardiazol and Cardiazol-Ephedrine in all forms of collapse, fainting fits, circulatory debility, myocarditis, *hypotension* (*after hæmorrhages*) and poisoning are reported by *Kese*. *Cima*'s experience with Cardiazol concerns, above all, *shock from serious burns*, acute cardiac dilatation due to physical overexertion, *traumatic shock*, syncope,

Apparent death from drowning

Friedländer has used Cardiazol (subcutaneously) in cases of apparent drowning and confirms the rapid and far-reaching effect of the preparation in states of collapse following swimming contests or protracted immersion after accidents. For the proper carrying out of Schäfer's method of resuscitation, *Schwarz* recommends Cardiazol as an adjuvant, stating that it is particularly indicated where life is acutely endangered because no overdosage need be feared. He uses Cardiazol especially in asphyxia of the apparently drowned. After a subcutaneous injection of 1 c.c. Cardiazol he causes carbonic acid to be inhaled with the air for the further excitation of the respiratory centre; respiration and consciousness return immediately. In the slighter cases, instillation of 20 drops of Cardiazol liquid had the desired effect. According to *Schwarz*, it would be useful if the physicians entrusted with the supervision of Public Baths, etc., were to draw the attention of their subordinates to the handling of Cardiazol injections for the prevention of death from drowning. To restore the respiratory function, *Rajna* injects Cardiazol even before artificial respiration is commenced and continues the medication at intervals of 10 minutes until normal respiration and circulation are re-established. *Dvořak* has also reported on the restorative action of Cardiazol in a case of apparent drowning. *Gusmão* recommends immediate venesection of the apparently drowned where pulse and respiration have stopped, an intravenous Cardiazol injection (1 c.c.) being given immediately after. *Thiel* also gives Cardiazol, etc., in the resuscitation of the apparently drowned.

commend intracardial injections of Cardiazol to restore the circulation after electric shocks or lightning accidents. The remedy is also used by *Gusmão* in that connection. *Dengl* describes a serious case of damage by lightning in which he gave Cardiazol, etc.

Injuries

The administration of restoratives in thoracic *gun-shot injuries*, followed by shock and serious cardiac embarrassment, is recommended by *Franz* who mentions subcutaneous injections of Cardiazol as one of the measures indicated. In *Schlomka*'s opinion, one should not hesitate to give intracardial injections of adrenaline, or failing that, of Cardiazol and similar substances, as an ultimum refugium in *commotio cordis*, in consideration of possible traumatic ventricular fibrillation.

H. Conrad advocates the prophylactic use of Cardiazol in the treatment of injuries requiring brief *ethyl chloride anæsthesia*. He injects Cardiazol before and after anæsthesia in intramuscular doses of 1 c.c. This procedure has resulted in a total absence of untoward incidents and patients take much less time to regain complete consciousness than usual.

J. Balneotherapy

E. *Müller* has tried Cardiazol with much success against *hydriatic "reaction"*. He began by giving 1 Cardiazol tablet once to twice daily. Some patients, who exhibited marked nervousness, were given 2 c.c. intramuscularly, improvement setting in practically immediately in every case. He also gave Cardiazol in *preparation for a course of baths*. He has reached the conclusion that

congelation, angina pectoris, anaphylactic shock following injections of antitetanic serum, *sunstroke*, drowning asphyxia, attempted suicide, *asphyxia due to exhaust-gases*, *lypothymic states* and *nerve-shock*. *L. Kraus* describes his very good results with Cardiazol in first-aid practice, e.g., in collapse, stenocardial attacks, poisoning by illuminating gas, narcotic substances (such as barbituric acid preparations), alcohol, carbon monoxide. *Schoen* states emphatically that every person attached to a first-aid organization should be practised in the use of cerebral analeptics such as Cardiazol, in accidents, suffocation, drowning, gas-poisoning, etc.

(b) Special cases

Congelations

According to *Katsch*, rubbing of the body with snow or wet towels, warming in a bath, should be supported by medicaments of the Cardiazol type. For the purpose of restoring frost-bitten people, *Grasmann* recommends intravenous injections of Cardiazol or similar substances.

Burns

Ullmann advocates the administration of Cardiazol (or Cardiazol-Ephedrine) several times daily, as an analeptic in shock following burns. *Riehl* also treated a case of burns in a 2-year-old child with Cardiazol, etc.

Injuries from electric currents or lightning

Cardiazol is among the remedies used by *Hofmann* in the treatment of electric shock. *Koelsch* gives intracardial injections, e.g., of Cardiazol, in these cases. *R. Müller* and *David* also re-

made it his practice to give Cardiazol also in cases where the Kauffmann test cannot for some reason be carried out before operation. Patients are given 1 Cardiazol tablet 3–4 times during the afternoon preceding the operation. *Küstner* has gained the impression that patients bear operative interference better where this medication is observed and he regards the introduction of Cardiazol as a cardiac and circulatory tonic before operations of great importance because it diminishes the risk of complications. The value of Cardiazol is all the greater because it is well tolerated, produces no uncomfortable sensations in the heart region and no states of excitation. Convenience of administration is another advantage. The method also diminishes, indirectly, the danger of post-operative ileus. *Schleipen* frequently causes his patients to be treated with Cardiazol before operation for the purpose of diminishing the likelihood of shock. *Esser* often gives Cardiazol prophylactically at the commencement of anæsthesia induction, especially in cases of hysterical neurasthenia and cardiac insufficiency. He finds that, with this medication, pulse and respiration remain in a satisfactory state throughout the entire operation. *Feriz'* observations also appear to confirm the prophylactic support of the heart given by Cardiazol (1 tablet, 3 times daily). His report stresses the fact that no case of post-operative cardiac collapse has been seen among obese or gravely cachectic patients where Cardiazol had been given prophylactically. *Bockenheimer* prepares the circulation by intravenous Cardiazol injections, e.g., before urgent operations; otherwise he gives it subcutaneously or per os in the liquid form for a few days before, and occasionally after, operation. The medication prevents a giving way on the part of the heart during operation, and complications apt to arise

no hydrotherapeutic course should be interrupted in the event of circulatory failure without Cardiazol having been given a trial first.

Fleury-Cuello draws attention to the good results obtained with Cardiazol in preparing patients for *carbonic acid baths.* Where the circulation shows signs of excessive exhaustion due to the baths, a matter of frequent occurrence in the beginning of balneological treatment, he again recommends Cardiazol.

SURGERY

A. Operations under general anæsthesia

I. Before operation

Cardiazol is among the vascular remedies recommended by *Seyderhelm* not only for states of collapse during or after operation, but also for the *pre-operative support of the circulation* of patients with sound hearts but with vasomotor instability. In the treatment of acute cardiac debility before operations, *Wachsmuth* favours Cardiazol. The remedy is recommended by *Ewald* for pre-operative administration where bradycardia exists. *Kappis* also mentions Cardiazol as one of the substances used by him for pre-operative support of the circulation. *Küstner* discusses cases in which Kauffmann's diuresis test revealed a disordered circulatory function. In these, he always gave 1 Cardiazol tablet 4 times daily for 2–3 days before operation. After this preparatory measure a second Kauffmann test established the restoration to normal circulatory conditions. (After operation, Cardiazol administration was continued for a few days per injectionem.) *Küstner* has since

as indispensable in the treatment of incidents during narcosis. *Ciminata* gives large doses of Cardiazol intravenously in anæsthesia mishaps. *Hesse* includes Cardiazol among the remedies to be given in *narcotic damage* (intravenously in acute, subcutaneously in milder cases). *Biedermann* mentions cases of narcotic damage due to accidental overdoses, in which Cardiazol produced a rapid and decisive effect on respiration and pulse. According to him, the Cardiazol effect is most conspicuous in serious collapse of operated persons. *Strasser* also speaks of excellent results with Cardiazol in complications arising during narcosis. The action of the remedy manifests itself almost immediately after a subcutaneous injection: respiration deepens and becomes regular, the pulse slower, blood-pressure rises and cyanosis is quickly abolished. It is also pointed out that Cardiazol can be repeatedly given at short intervals. *Kemkes* also uses Cardiazol in the treatment of narcotic damage (2 c.c. subcutaneously, every 3–6 hours, during the first 24 hours).

Esser's experience concerns mainly *asphyctic attacks* and oxygen apnœa (Roth-Draeger apparatus) occurring during anæsthesia. Calm and deep respiration followed the injection in every case. The action was especially prompt in the initial stages of asphyxia, but an intravenous Cardiazol injection restored the pulse and calm, deep respiration immediately also in fully developed asphyxia (radial pulse no longer palpable, maximal dilatation of pupils, cessation of breathing). The operation could then be finished without any further untoward incidents. In respiratory paralysis, *Monteiro* gives subcutaneous or intravenous injections of analeptics, including Cardiazol. *Barbera* likewise refers to the intravenous use of Cardiazol, etc., in respiratory paralysis occurring during narcosis. *Jagić* is another writer mentioning Cardiazol

through faulty circulation after anæsthesia are avoided. Patients over 50 years of age with slight relative hypotension are treated by *Röpke* with Cardiazol, etc., for the prophylactic strengthening of the vascular tone. *Monteiro* gives his patients 1 or 2 Cardiazol injections before and after operation.

Lanz recommended Cardiazol for the preparation of patients for *goitre operations*. *Feriz* observed that the pulse curve in Graves' disease, above the temperature curve prior to Cardiazol medication, fell below the temperature curve already on the first day after operation and remained low during the critical period. On the third day the pulse curve fell below the pre-operative level, absorption fever notwithstanding. This was a common observation in all Basedow cases. *Payr* also gives 3—4 Cardiazol tablets daily prior to Basedow operations where cardiac debility exists.

Pflomm, in his *tropical practice*, gives 3 doses of 20—30 drops of Cardiazol on the day before operation and has not had a single case of post-operative beri-beri shock from the time that he has followed this method. In cases requiring immediate operation, he gives 1 or 2 Cardiazol injections during operation even though his patients' hearts may appear to function normally. *Virnich* advocates prophylactic Cardiazol injections for feeble patients of advanced age, especially if an operation coincides with hot weather.

II. During Operation

(a) In incidents during narcosis (narcotic damage, asphyxia, circulatory disturbances, etc.)

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pheral vessels (see also Vascular block, p. 46), and thus disburdens the heart to a considerable extent. In view of the rapid onset of its action Cardiazol is pre-eminently indicated in the treatment of shock. In grave surgical shock (75 cases), *Schlaepfer* administered 1–2 c.c. Cardiazol at intervals of 1–3 hours, frequently in alternation with digitalis, during 24–48 hours, apart from subcutaneous or intravenous infusions of normal physiological salt solution or glucose solution. Even desperate cases reacted to this combined treatment with a lower pulse frequency, deeper and less frequent respiration. In some cases, pre-operative Cardiazol treatment sufficed to prevent post-operative shock. Where pre-operative administration of Cardiazol was not feasible, the remedy was injected immediately after operation, at intervals of 1 hour or more, the result being equally satisfactory. The advantages of Cardiazol connected with its prompt action where there is risk of shock are also emphasized by *E. Schneider.*

(b) Special anæsthesias:

Rectal anæsthesia

To combat incidents during rectal narcoses, *Schulte* advocates the intravenous use (i.a.) of Cardiazol as an antidote. Cardiazol is also among the medicaments used by *Eichenberg* in the treatment of circulatory disturbances. Where necessary, prophylactic circulatory tonics, e.g., Cardiazol-Ephedrine, are administered simultaneously with the rectal anæsthetic. In marked circulatory debility in children during rectal narcoses, *Sievers* gives Cardiazol apart from hypertonic remedies with a peripheral action. *Domanig* states that Cardiazol, given intravenously in doses of 2–3 c.c., accelerates and deepens respiration very distinctly. Also *Hesse*

among the respiratory excitants useful in surgery and stressing the harmlessness of overdosage.

According to *Schleipen*, Cardiazol renders good services not only in *circulatory weakness* due to a failing heart function, but also in peripheral circulatory debility (due to vasomotor disturbances or loss of blood), a condition of some concern to the surgeon. The Cardiazol effect in serious traumata is seen in a marked rise in the blood-pressure, an immediate improvement in the quality of the pulse and an increase in its frequency. In the treatment of *operative collapse*, *Kappis* generally uses Cardiazol. In peripheral vascular paralysis, he administers adrenaline with glucose solution + Cardiazol. To stimulate respiration, he gives Cardiazol in the first place. *Simon* also, first of all, gives intravenous or subcutaneous injections of Cardiazol (1–2 c.c.) in collapse during operations. Where the state of collapse is protracted, he finds intravenous continuous infusions (0·9% saline solution, Normosal*) with an addition of Cardiazol, Digipuratum (Knoll), etc., especially efficacious. *Hernández Ramírez* describes a case of uranostaphyloplasty with 3 successive attacks of syncope, each successfully fought with 1 c.c. Cardiazol (the last by intracardial injection). Cardiazol figures among the remedies described by *Schoen* and *Gros* as the preparations of choice with which to render the circulation equal to the extra strain placed upon it by narcosis. They prevent vascular collapse and counterbalance toxic paralyzing effects. According to *Holzbach*, a weak heart demands support in *surgical shock* to enable it to stand up to the increased resistance in the peripheral regions (the distinction, in his view, between shock and collapse). The necessary support is ideally supplied by Cardiazol as it abolishes the resistances in the peri-

(c) Interruption of the narcotic state

Behrend reviews about 400 cases of overdosage in rectal Avertin*- as well as in Pernocton*- and Evipan*-narcoses in which he administered Cardiazol where it was necessary to *rouse* patients from the narcotic state or to set the respiration going again. He attained his object by giving Cardiazol in high dosage: 3–10 c.c., slowly administered by the intravenous route; in some cases, up to 15 c.c. was given in one dose. As soon as the rousing action became manifest, the rest of the injection was administered subcutaneously or intramuscularly. No damage followed these large Cardiazol doses, least of all epileptiform symptoms. *Convulsions occurred only in a single case, one of operation on the* brain. (Attacks of convulsions can be prevented by the addition of glucose and calcium solutions.) The rousing effect of Cardiazol has been tested by *Pieniezny* in 96 cases (58 of ether-, 35 of Evipan*- and 3 of Avertin*-anæsthesia). The Cardiazol injections were given immediately after operation and exclusively by the intravenous route, patients being closely observed during the following 30 minutes. In the majority of cases, the first noticeable effect was an increase in the respiratory volume which ensued already during the (very slowly performed) injection. The respiratory frequency also rose in many cases. The pulse at the same time grew stronger and its action distinctly more regular. Infusions of physiological salt solution, for which preparation had been made in a few particularly grave cases, proved unnecessary. The rousing effect of Cardiazol was more marked in patients under 50 than those over that age, but the post-narcotic sleep was *shortened in all cases* with a corresponding diminution of aspiration risks. The action on respiration and circulation was never

mentions that Cardiazol may be given in high dosage in paralysis of the circulatory and respiratory centres.

Colmers says that where rectal narcosis is combined with local anæsthesia, lobeline, . . . and Cardiazol, in 3 c.c. ampoules, should always be kept at hand during the operation for the purpose of counteracting respiratory or circulatory disturbances should they arise.

Intravenous anæsthesia

In an incident during narcosis, *Redmann* used Cardiazol (1 c.c., intramuscularly) in addition to several other antidotes. *Schwab* was able to save two patients in a state of dangerous collapse by the immediate injection of Cardiazol and lobeline. *König* says that excitants of the respiratory centre, such as Cardiazol, are requisite in practically all incidents during narcoses. Lobeline plus Cardiazol, etc., are also used by *Vogt* on occasions of brief intravenous narcosis to restore patients from incidental debilities. Also *Kauffmann* recommends the intravenous administration of 3 c.c. Cardiazol in incidents during injection narcoses. *Bennett* includes Cardiazol among the antidotes to be given on these occasions. *Picco* and *Zanetti* report that respiratory disturbances during injection narcoses were immediately abolished by a few injections of lobeline, Cardiazol, etc., and that the narcoses subsequently ran a normal course. *Kaufmann* reports that asphyxias and circulatory disturbances, which figured as incidents in several cases, were quickly abolished by Cardiazol, etc. *Gandow* also had a case of asphyxia during injection narcosis which so improved after Cardiazol and lobeline administration that the operation was able to be carried out without further trouble.

dependent on the dosage employed. A number of patients awoke from deep narcosis immediately after the Cardiazol injection and after a few minutes were able to understand questions and to answer them coherently. In others, the injection was promptly followed by a deepening of the respiration, a heightened muscular tone, spontaneous movements, return of the corneal reflex, and, shortly after, the waking state. Still others, whilst not reacting to painful stimuli, showing no influence on the lowered muscular tone and awaking only after a relatively long time, yet exhibited an unmistakable reaction to Cardiazol in that respiration became deeper, slower, and more regular after the injection. Respiratory improvement was, in fact, present in all the 15 cases registered as positive. No effect from Cardiazol was observed in 5 cases, 4 of which had only received 3 c.c. Particular stress is laid on the fact that even large intravenous Cardiazol injections (6—9 c.c.) have never produced incidents or convulsions. *W. Meyer* describes over 100 instances of narcoses in which he used Cardiazol as a rousing agent, the anæsthetics being ether, Evipan*, Eunarcon*, Avertin* and Eukodal*-scopolamine. He found the optimal dose to be 3 c.c., administered by intravenous injection; also with the most profound narcotic states. The results were quickest and most conspicuous in narcoses induced by intravenous injections of Eunarcon* and Evipan*, without additional narcotics. In the 40 cases of this description, patients awoke almost instantaneously, often already during the progress of the slowly performed intravenous injection. The action was seen in a better perfusion of skin and mucous membranes, slow movements of the arms and a raising of the body on the operating table. Within 5—10 minutes after the injection, patients were fully conscious and completely

absent. In some cases patients awoke immediately after the injection and in some even during injection. They opened their eyes, raised or turned their heads and occasionally spoke a few words. They soon relapsed into sleep which, however, no longer resembled a narcotic sleep. The rousing dose, originally 5 c.c., was later reduced to 3 c.c., which lower dose proved sufficient in the majority of cases. The impression was gained that the Cardiazol action is best in Evipan* narcosis, but very distinct also in ether anæsthesia. *Pieniezny* had only a single case of untoward secondary effects from the Cardiazol injection (twitching, suspended respiration), an isolated instance to which no significance is attributed. *Fuge* writes that Cardiazol is a very suitable agent to rouse patients from narcosis, or from the after-sleep if it is for any reason desired to shorten the latter. His previous knowledge of Cardiazol determined him to use it in the above connection and he gave it not only where there was reason to fear incidents owing to narcotic overdosage, but also in a number of cases of Evipan* anæsthesia with an abnormally long after-sleep. The results were always satisfactory. *Fuge*'s practice is to inject 3 c.c. Cardiazol carefully and very slowly by the intravenous route. Patients often wake up whilst the injection is still proceeding; the blood-pressure is rarely altered. In a few cases, a rise of 5–10 mm. Hg. has been seen but a return to normal values ensued shortly after. The pulse frequency, on the other hand, increases slightly and the pulse grows fuller. Motor restlessness has not been witnessed after Cardiazol injections. Also *G. Schäfer* gives Cardiazol to rouse patients from narcoses induced by various anæsthetics. He injects 3–9 c.c. very slowly by the intravenous route. The rousing action was found to be subject to individual fluctuations, the latter again

had been given in addition. Only 5 cases failed to respond visibly to Cardiazol. The best results were seen in Eunarcon* narcoses. Marked improvement in respiration was invariably observed immediately after the Cardiazol injection, also a favourable influence on the circulation. Harmful secondary effects were never met with. It is certain, moreover, that a shortening of the narcotic state diminishes the risk of pulmonary and circulatory complications. *Schlaepfer* used Cardiazol in 175 cases of Avertin* anæsthesia to shorten the narcotic sleep. Where there were reasons for waking patients within $^1/_2$–1 hour after operation, 2 c.c. Cardiazol was given intravenously by slow injection. About 10 minutes after that injection, patients began to move, periods of sleep still intervening. A second injection of 2 c.c., given 30 minutes after the first, then led to gradual and, finally, complete waking. Another method used was to inject 2 c.c. Cardiazol intramuscularly immediately the operation was finished. This resulted in deeper and regular respiration and normal cardiac activity. With this method 2–5 hours elapsed until patients were completely awake. Cardiazol is mentioned also by *Frey* among effective rousers from excessively deep Avertin* sleep. *Blacher* is in the habit of administering Cardiazol in a 25% grape-sugar solution, intravenously, to provoke a quicker waking from Evipan* narcosis. In a number of cases of Eunarcon* anæsthesia, *Fuge* tried to hasten his patients' waking by giving them intravenous injections of Cardiazol (3–5 c.c.). He recommends this method especially where patients have been subjected to short anæsthesia induced by 4–5 c.c. Eunarcon* in the consulting room. The intravenous injection of Cardiazol effects an almost instantaneous waking whilst undesirable secondary effects are completely absent. *Wood* has carried out systematic

aware of their situation. The rousing action was clearly observed also in all cases where Eunarcon* or Evipan* anæsthesia was supplemented by ether. After an intravenous injection of 3 c.c. Cardiazol, patients awoke from the state of complete relaxation and absent reflexes within a few minutes. Cardiazol also succeeded in hastening waking from pure ether narcoses. The intravenous injections were made when certain symptoms showed that the deepest narcotic stage had been passed. Cardiazol was injected in the same manner for the purpose of improving respiratory and circulatory activity and of promoting a quick transition from the narcotic to normal sleep after the use of Avertin* as the basal narcotic. In some cases, a further intravenous injection of 3 c.c. Cardiazol was necessary about 40 minutes later to rouse patients quickly from the Avertin* sleep. *Stumpf* also publishes a record of 100 cases in which he injected Cardiazol to shorten or interrupt narcoses induced by Eunarcon*, ether and Avertin*. He injected the Cardiazol always as soon as the operation was finished, mostly 3 c.c. intravenously, followed at once by a further 2 c.c. subcutaneously in cases of Avertin* narcosis. Of 15 patients who were given Cardiazol after Eunarcon* anæsthesia, 11 awoke immediately, 2 others after 10 minutes, and the rest after 15 minutes. In the case of ether narcosis, 4 patients awoke immediately after injection, 6 after, at most, 25 minutes, and 8 after, at most, 1 hour after the injection of Cardiazol. Whilst nearly all patients not treated with Cardiazol after Avertin* narcosis exhibited no reflex action for up to 2 hours, 66 patients had their post-narcotic sleep (otherwise exceptionally long in such cases) considerably shortened by Cardiazol. These were cases with a relatively prolonged narcosis, especially since ether, to the extent of 50–160 gm.

tory disturbances. The simultaneous influence on respiration is another factor which must not be underestimated. *Biedermann* advocates the use of Cardiazol more particularly in states of collapse following lengthy operations. *Boegel* reports that a subcutaneous injection of 1 c.c. Cardiazol greatly improves the clinical picture of patients coming from major operations with an irregular pulse and unsatisfactory respiration, in a very few minutes. In cases of this sort, the Cardiazol medication was continued for some days. *Meinhard* also gives Cardiazol post operationem; his impression is that the injection of 1 ampoule Cardiazol immediately after operation and another $^1/_2$ hour later, brings the patient's circulation back to a normal state more rapidly than any other known method. The remedy apparently also deepens respiration, shortens and eases the post-operative narcotic period; patients take less time to wake up; there is less tendency to retching and vomiting and greater freshness than customarily seen. On account of these agreeably surprising properties of Cardiazol it is now used regularly after general anæsthesias, regardless of the method by which they are induced. *Esser* describes the marked improvement seen immediately after a subcutaneous Cardiazol injection in a number of cases of post-operative cardiac insufficiency and states of collapse. *Ruef* continues with Cardiazol at intervals of 1 hour after lengthy major operations where followed by gradual failure of the heart function: improvement of the pulse ensues promptly and in view of the excellent general influence of the remedy, an injection is made every 4 hours during the first 24 hours following an operation. *Jemec* tried Cardiazol in the case of patients reacting to protracted narcosis with a feeble pulse or collapse. Within 3–4 minutes after a subcutaneous injection the

trials in the denarcotization of anæsthetized patients and speaks of Cardiazol as an efficacious and convenient remedy. Among the rousing agents mentioned by *Döhring*, Cardiazol occupies the first place. The preparation is used as a rousing agent also by *Simon* (3–5 c.c., intravenously). He finds that the operated patient again reacts to stimuli after a few minutes and is soon conscious.

III. After Operations

According to *v. Bergmann*, much benefit has been obtained from Cardiazol, in addition to autotransfusion, in grave *post-operative circulatory disturbances. Denning* also includes Cardiazol among the remedies to be given against post-operative circulatory insufficiency and *Strassmann* likewise administers it in post-narcotic circulatory upset. *Melchior* considers it advisable to resort to circulatory prophylaxis (5 c.c. camphorated oil, intramuscularly, or Cardiazol in 1 c.c. doses, subcutaneously or intramuscularly, every 2–3 hours) in all major operations as soon as the operation is over. *Kappis* gives Cardiazol, etc., to combat post-operative shock or collapse. *Orator* and *Straaten* also use it in cases of post-operative circulatory collapse. *Siebner* states that Cardiazol is, above all, insuperable in the treatment of post-operative states of collapse. Among his cases was one of acute cardiac debility which occurred on the 5th day following choledochotomy and probably caused by cholæmia. He speaks of the life-saving action of Cardiazol after all antidotes had failed. An intravenous injection of 1 c.c. Cardiazol set the circulation going again and this treatment, in combination with intravenous Normosal*-adrenaline infusions, enabled the patient to survive the collapse. The favourable influence of Cardiazol was conspicuous also in other acute circula-

Breitner administers the remedy after *Basedow operations.*

Orator and *Straaten* add Cardiazol to hypnotics given against post-operative insomnia.

Schleipen is emphatic on the point that *thrombosis* has been *unknown* among his many Cardiazol-treated cases. *Janson* confirms the opinion that intravenous injections of preparations such as Cardiazol are unlikely to provoke thrombosis.

(Prevention of post-operative thrombosis and embolism by Cardiazol-Quinine is discussed on page 188.)

Addendum: *Blood transfusion*

After blood transfusions, *Kiss* administers 10 c.c. of a 20% dextrose solution with an addition of 1 c.c. Cardiazol or similar substance. *Dutton* recommends the administration of 1 c.c. adrenaline (1:1000) or intravenous injections of Cardiazol every 20 minutes in collapse occurring during blood transfusions until the state of collapse is remedied.

B. Operations with local anæsthesia

I. Lumbar or spinal anæsthesia

In cases of collapse during operations carried out with lumbar anæsthesia, *Boegel* gives intravenous Cardiazol injections of 1 c.c. This results in immediate improvement which is then maintained by further subcutaneous or oral doses of Cardiazol so that many patients feel no after-effects from the lumbar anæsthesia. In less urgent cases, a subcutaneous injection answers the purpose. Its effect is seen within 5 minutes. *Biedermann* also recommends Cardiazol in states of collapse following lumbar anæsthesia. *Popoviciu*

pulse was again palpable and respiration deepened. *Schleipen* tells of very favourable results from Cardiazol in post-operative collapse and regularly uses the preparation as an addition to the customary infusions in the after-treatment of operations. *Baumann* also recommends Cardiazol as an addition to glucose infusions in post-operative treatment.

Ruef speaks of his observation that *respiratory disturbances* following narcosis are beneficially influenced by Cardiazol. *Orator* and *Straaten* have *successfully treated dangerous asphyctic attacks* during the final narcotic stage with Cardiazol, etc.

Post-operative lung complications (bronchopneumonia, infarct) were treated by *Boegel* with Cardiazol in combination with 1% morphine, the result being a deepening of the respiration. Among the remedies recommended by *Stahnke* for the treatment of post-operative lung complications, Cardiazol figures prominently and is mentioned also by *Staehelin* as one of the medicaments indicated in post-operative pneumonia. *Orator* and *Straaten* likewise give Cardiazol, etc., in post-operative bronchopneumonia. According to *W. Meyer*, Cardiazol is particularly suitable also for the prevention and treatment of post-operative pneumonias in which it improves ventilation and circulation during and after anæsthesia. *Simon* gives Cardiazol and Digipuratum (Knoll) the preference in post-operative bronchopneumonias.

In the treatment of *post-operative peritonitis*, *Sigwart* and *Kappis* advocate Cardiazol (i.a.) as an adjuvant.

Cervenansky regards the intravenous injection of circulatory tonics such as Cardiazol (together with glucose) as an important measure against *post-operative ileus*, to be resorted to at the first signs of possible intestinal occlusion.

as a prophylactic measure in every case, whether local or general anæsthesia is employed. During his 6 years' use of this method he has had no case of collapse or other contretemps, common enough before the advent of Cardiazol.

Barbera advocates the use of Cardiazol and similar substances in susceptibility to scopolamine.

(On the detoxicating action of Cardiazol on local anæsthetics, see page 29.)

Addendum: *Infantile surgery*

Parfanowicz has had very good results with Cardiazol (apart from artificial respiration) in cases of suspended respiration and of cyanosis due to *overnarcotization*; as a consequence he now gives the remedy before anæsthesia as a prophylactic measure which ensures calm and steady breathing on the part of his little patients during operation. Cardiazol has also proved of excellent service in all forms of *shock* and *traumata*. In 8 cases of acute appendicitis, a prophylactic injection of Cardiazol, 15 minutes before, and a second injection after the laparotomy, successfully countered the hypotension and increased frequency occasioned by the operation. In *osteomyelitis*, Cardiazol was given for weeks, pulse and blood-pressure remaining perfectly normal, pyrexia notwithstanding. In 11 cases of *pyothorax*, both circulation and respiration were favourably influenced which much facilitated the labour of the thorax and exhaustion of pus. *Post-operative pneumonia* is another field in which the writer uses Cardiazol. By stimulating the circulation and respiratory organs, it enhances the power of resistance in operated patients. *Veicstein* gives Cardiazol to children *prophylactically before operations* under chloroform

uses Cardiazol prophylactically to tone up the circulation for operations, especially those performed with spinal anæsthesia. Patients are given 15 drops Cardiazol thrice daily for 3 or 4 days before operation, and 1 ampoule each Cardiazol and caffeine 20 minutes before anæsthesia; if necessary, another 1 or 2 ampoules Cardiazol at a later stage. The result of the method is marked improvement in the general condition, more especially a stronger heart and *quieter and deeper respiration. Cardiazol is also successfully used* in post-operative complications. The same author stresses its harmlessness which enables it to be given in large doses and at short intervals without deleterious effects of any kind. *Papp* and *Tepperberg* recommend the intravenous administration of substances such as Cardiazol where patients show slight indisposition during the first 20 minutes of spinal anæsthesia. *Aievoli* also resorts to Cardiazol, etc., to combat the symptoms of hypotension occurring during spinal anæsthesia.

(Numerous writers draw attention to Cardiazol-Ephedrine as a particularly useful combination with which to combat or prevent disturbances provoked by spinal anæsthesia. See page 230.)

Addendum: *Lumbar puncture*

Hypotension after lumbar puncture is treated by *Kappis* by intravenous injections of Cardiazol, etc.

II. Local anæsthesia

In collapse occurring with local anæsthesia, *Mandl* gives circulatory stimulants, preferably Cardiazol. *Deichmüller*, who uses local anæsthesia for the majority of his operations, injects, on the strength of his experience, 2 c.c. Cardiazol subcutaneously

In these and in cases of collapse after lengthy operations, much loss of blood and narcotic damage, Cardiazol proved superior to all other medicaments. A further remarkable advantage of Cardiazol, of special importance for operative gynæcology, is the *absence of a paralyzing influence on the smooth musculature.* It is for this reason that *G. Conrad* favours Cardiazol as a circulatory remedy after gynæcological operations with their well-known tendency to cause intestinal paralysis. *Hellendall* describes the life-saving action of Cardiazol in a case of post-operative cardiac insufficiency (total extirpation, after Döderlein). Pulse and respiration had steadily deteriorated in spite of all previous therapeutic steps (physiological salt infusion, continuous drop-infusion, camphor, digitalis, caffeine). The case gave cause for grave anxiety. Cardiazol was then injected subcutaneously, apart from caffeine and digitalis, 2 injections being made with an interval of 3 hours. After $1^1/_2$ hours there was a distinct turn for the better. 5 further Cardiazol injections were given during the following 8 hours, apart from caffeine and digitalis. The previously alarming state of debility was by then greatly improved. *Galve Raso* gives Cardiazol to support the circulation in laparotomies for the reason that it does not interfere with the intestinal function: there is no paralyzing influence on the smooth musculature, always somewhat slack after gynæcological interference. Pulse and general condition were much improved by a Cardiazol injection also after lengthy and gravely exhausting operations, the improvement being subsequently maintained by further Cardiazol injections administered every 2 or 3 hours. *Galve Raso* gives Cardiazol also in minor operations or examinations, for the purpose of preventing or combating attacks of syncope provoked by pains or fright.

anæsthesia, and to combat incidents and operative shock during and after operations. His rule is to give his young patients $^{1}/_{2}$ to 1 ampoule Cardiazol 10 minutes before inducing anæsthesia, or to prepare them by oral doses of $^{1}/_{2}$–1 c.c., given 3–4 times daily during 1 or 2 days. The favourable influence of the preparatory Cardiazol treatment was clearly established by means of controls not treated with Cardiazol. Narcotic damage in the latter was always quickly countered by subcutaneous injections of 1 c.c. Cardiazol. The preparation proved useful also in cases of belated waking and of *anæsthetic after-effects.* In surgical disorders (phlegmons, empyema, osteomyelitis, etc.) Cardiazol was repeatedly given subcutaneously and, subsequently, per os, as long as the patients' state necessitated the medication. The effect of Cardiazol manifested itself invariably in a stronger pulse, a more satisfactory blood-pressure and a quieting of the respiration. According to *Sindler*, energetic injection treatment with Cardiazol serves to maintain the circulation adequately in *collapse* occurring during operations on children with grave circulatory disturbances (resection of ribs, arteriotomy, etc.). *Eckstein* refers to the prompt recuperative action of Cardiazol in post-operative collapse after surgical treatment of pylorospasm.

GYNÆCOLOGY AND OBSTETRICS

A. Gynæcology

Gynæcological operations

G. Conrad has administered Cardiazol to over 50 patients, mostly operation cases, and some women admitted to the ward with sepsis post abortum sive partum complicated by heart and lung troubles.

Cardiazol is also recommended by *Hammerschlag* against eclampsia where the pulse is small and frequent.

Vogt administers Cardiazol in the treatment of nephropathies (*pregnancy toxicoses*).

II. Parturition

Cardiovascular disturbances

Sachs mentions Cardiazol among the remedies used by him to support women with feeble hearts during parturition and the remedy is recommended by *Kraatz* as a central vasomotor excitant in heart disorders during labour. To afford direct support to the heart he gives strophanthin. *Esch* treats compensation irregularities during parturition with intramuscular or intravenous injections of Digipuratum (Knoll). In addition, he gives injections of Cardiazol at intervals of 1–2 hours whereby the vasomotor centre is lastingly excited, a factor of special significance in view of the danger threatening from the change in the circulation during the after-birth period. *Stark* gives an intravenous or intracardial injection of Cardiazol in collapse of parturient women. *Schultz* treats birth-shock with camphor or Cardiazol, as cardiovascular remedies.

Lehner has frequently given prophylactic injections of Cardiazol during obstetric Rectidon*-twilight sleep in the expulsive stage.

In a case of collapse following child-birth, *Rauter* injected 2 c.c. Cardiazol intravenously; about 2 minutes later, respiration returned and the pulse was again palpable. A relapse occurring, a further intravenous injection of 2 c.c. Cardiazol again improved the condition quickly. In another case, the patient had suffered

Dysmenorrhœa

In a case of dysmenorrhœa with severe abdominal pains and temporary loss of consciousness, *Steminer* administered Ephedralin* and Cardiazol with the result of considerable improvement in the general condition.

(The combination-product "Cardiazol-Dicodid" has proved particularly useful in dysmenorrhœa treatment. See page 209.)

Pyrexial treatment of gonorrhœa

Janson has had good results from intravenous Cardiazol administration in a case of collapse during pyrexial treatment of gonorrhœa in a female patient.

B. Obstetrics

I. Pregnancy

Cardiovascular disturbances

In decompensation during pregnancy, *Burckhardt* orders his patients to bed and at once administers digitalis preparations and Cardiazol (amongst other remedies) where pulmonary complications make their appearance. *Esch* advocates injections of camphor or Cardiazol at intervals of 1—2 hours in circulatory disturbances during the period of gestation, in addition to digitalis treatment. *Moritz* gives Cardiazol, etc., in serious cardiac insufficiency during pregnancy.

Eclampsia, pregnancy toxicoses

Vogt favours the administration of Cardiazol, etc., in serious cases of *eclampsia* to afford timely support to the circulation.

Cardiazol is also recommended by *Hammerschlag* against eclampsia where the pulse is small and frequent.

Vogt administers Cardiazol in the treatment of nephropathies (pregnancy toxicoses).

II. Parturition

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a third degree peritoneal tear and had lost blood to an alarming extent. She received an intravenous injection of 2 c.c. Cardiazol which instantly improved her condition.

Gremme administers Cardiazol in acute *pulmonary œdema* during labour. *Torres* also describes a case of pulmonary œdema after parturition in which a Cardiazol injection caused the entire symptom complex to disappear.

Secondary feebleness of labour

In secondary feeble labour where the fœtal heart-sounds are bad, *Abel* gives Orasthin* together with 1 c.c. Cardiazol. *Gamstätter* was able to accelerate delivery considerably by the simultaneous administration of Thymophysin* and Cardiazol during the second half of the dilatation period, and during the expulsion stage. After a series of experiments, it was found that the best and most uniform results followed a dose of one-third c.c. Thymophysin* + 1 c.c. Cardiazol, injected intramuscularly in the mixed syringe. With primiparæ it was occasionally necessary to follow up the first injection with another one-third c.c. and sometimes also the last third of the content of a Thymophysin* ampoule. The prompt onset of more energetic labour pains resulting from the combined injection was very striking. In primary or secondary feebleness of labour *Moragues Bernat* combined the ecbolics with intravenous or intramuscular injections of Cardiazol. This method results in a favourable influence also on the fœtus. Where antispasmodics are required he regards the combination with Cardiazol, etc., as indicated to prevent a possible paralyzing action of the antispasmodic on the fœtal heart (see also p. 124).

Intra-uterine asphyxia (or diminution of fœtal heart-sounds)

Vogt advocates injecting the parturient mother with 1 c.c. Cardiazol (or caffeine) once or twice, in order to prevent intra-uterine asphyxia by stimulating the action of the fœtal heart and simultaneously exciting the respiratory centre. *Hammerschlag* recommends Cardiazol injections to be given to the mothers (repeatedly if necessary) in cases of intra-uterine asphyxia. The medication also supports the fœtal cardiac action. According to *Poeck*, intravenous injection of Cardiazol is beneficial in intra-uterine asphyxia, at times also direct injection into the still intra-uterine fœtus. *Poeck* has treated 39 cases in this manner, 37 of the children being born alive. *Čížek* used Cardiazol intravenously in 14 instances of threatening intra-uterine asphyxia. The heart-sounds, down to 90–60 prior to the Cardiazol injection, increased by 40–80 beats within 2–3 (rarely as much as 5) minutes. In 2 cases only was no improvement achieved. *Čížek* concludes that Cardiazol injections promise success where it is a question of transient alterations in the fœtal heart action apparently necessitating operative interference. The treatment (especially during the second stage) *reduces the occasions for operative termination of labour in favour of conservative treatment:* but even where operation cannot be avoided the heart-sounds can be temporarily improved by Cardiazol until the conditions for operative interference have become more favourable. *Rodecurt* publishes his experience with Cardiazol in 100 cases of intra-uterine asphyxia. The remedy was administered to the mother by subcutaneous injection. Complete success was obtained in 40 cases, in the spontaneous delivery of living infants. In 20 other cases, the medication was relatively successful inasmuch as valuable time was gained by the Cardiazol

injection for the preparation of operative delivery. Among the 40 negative cases there were 12 with circulatory inhibition in the umbilical cord, and 4 with cerebral hæmorrhage. *Rodecurt,* therefore, advocates the use of Cardiazol in every case of asphyxia intra partum and even for prophylactic purposes. *Stahnke* has used Cardiazol for some years in the treatment of asphyxias intra partum and has had many opportunities to convince himself of its efficacy. He feels certain that he has saved a considerable number of asphyctic infants during the first stage whilst, in the second stage, many patients have been spared operation. 1 c.c. Cardiazol, subcutaneously administered to the mother, gave very prompt and reliable success in practically all asphyxia cases. Where the injection brings no improvement in the course of 5—10 minutes, or the state of asphyxia persists, there is every probability of some complication (mechanical, cerebral hæmorrhage, etc.) necessitating operative interference. *Moudrý* has tried Cardiazol in 310 grave and 290 slighter cases of intra-uterine asphyxia and places on record that a favourable effect on the incipient asphyxia was obtained in 75% of all cases. Although those of the first group were of a very grave nature, the Cardiazol medication yet brought about spontaneous birth in more than half the cases. In the slighter forms, Cardiazol always produced a prompt and *lasting regularization of the heart-sounds. Moudrý,* therefore, invariably makes prophylactic use of Cardiazol in all cases of pelvic presentation, especially in protracted delivery and during the expulsion period. Infants born with grave asphyxia were completely resuscitated by Cardiazol within 5—10 minutes after birth. *Nevinny* states that the use of Cardiazol in cases of *pelvic presentation* reduces infantile mortality very considerably.

He gives prophylactic injections of Cardiazol into the pelvis of the unborn fœtus. Where the fœtal heart-sounds are good, 0·3 to 0·5 c.c. Cardiazol is not injected until the nates appear. In urgent cases, injection into the visible part, as into the foot in foot-presentation, is preferred. It is proved by statistics that since the use of Cardiazol was adopted the mortality among infants born in pelvic presentation has declined from 10–15% to 5·38% (or, if those weighing more than 2000 gm. are included in the calculation, to 4·13%). Where complications ensue (threatening deterioration of the fœtal heart-sounds during the first stage or at the commencement of the expulsion period) the mothers are first treated with intravenous Cardiazol injections. Apparently Cardiazol has also a favourable influence on possible spasmophilia of the os uteri and prevents vaginism. *Genth* also reports good effects from the injection of small amounts of Cardiazol into the fœtal buttocks in pelvic presentation shortly after the commencement of delivery. *Krauss* speaks of good results from direct Cardiazol injection into the fœtus where the latter's life is endangered. *Kieser* reports that Cardiazol enabled him to obtain prompt improvement of the cardiac function in intra-uterine asphyxia, giving him time (occasionally with the aid of a further injection) to prepare for surgical assistance.

In uterine relaxation Cardiazol is also used with much advantage, in certain cases in *combination with hypophysis preparations*, which latter are rendered less dangerous by Cardiazol. *Fecht* favours an intramuscular injection of 1 c.c. Cardiazol to the mother about 10 minutes before the Thymophysin* injection. He also finds that the opening stage is still further shortened by the combined Cardiazol-Thymophysin* treatment. In the expulsion

stage, the power of the parturient woman is undoubtedly increased by Cardiazol, the pains showing greater constancy and the expulsion of the fœtus being accelerated. Also *Hüssy* writes that hypophyseal preparations can be combined with Cardiazol in the same manner as quinine in order to prevent a possible lessening of the fœtal heart-sounds.

According to *Bachner* it is worth while attempting to counter the diminution of the fœtal heart-sounds (change in fœtal circulation on fœtal head entering pelvis) by means of chloroform inhalation and Cardiazol. Also *Uter* is of opinion that subcutaneous or intravenous Cardiazol injections administered to the mother at that stage must have a beneficial effect on the fœtal circulation.

Obstetric operations

Sztehlo invariably administers 1 c.c. ephedrine + 1 c.c. Cardiazol after *Cæsarean section*. This medication has not only proved beneficial as a tonic for the maternal heart but also as an excitant of the fœtal circulation. From the time of the introduction of Cardiazol, now regularly employed, the infants are readily lifted from the uterus and, in most cases, begin to cry immediately. In premature extrusion of the placenta following uterine incision, *Vogt* gives intravenous continuous drop infusions of a 5% Calorose* solution with an addition of Cardiazol, Digipuratum (Knoll), strophanthin, etc., to assist blood transfusion.

Artificial abortion

Kayser describes Cardiazol as suitable for the treatment of acute cardiac paralysis during artificial abortion.

Addendum: *Asphyxia neonatorum*

Manicatide mentions Cardiazol among the remedies useful in the treatment of asphyxia neonatorum. *McIlroy* recommends it as a stimulant in white asphyxia. *Jost* has for some considerable time given Cardiazol in 1–2 c.c. doses in asphyxia neonatorum and speaks of the prompt action of the remedy which frequently ensues after about 5 minutes. *Brümmer* refers to about 20 cases of, mostly grave, asphyxia which gave him the opportunity to convince himself of the excellent effects of Cardiazol. His rule is to inject $^1/_2$ c.c. Cardiazol subcutaneously into the immediately separated infants whose heart-sounds are barely audible or greatly retarded, the measure being preceded by tracheal catheterization (removal of possibly aspirated matter from the trachea). Within 2–5 minutes after the injection the action of the heart was, generally, improved to a surprising extent. Heart-sounds of a frequency of 80 or less soon increased to 100–120. Previously very faint sounds became distinct and more frequent; respiration also improved in many cases. *Louda* describes a case of asphyxia neonatorum. Treatment of mouth and nose by suction was followed only by sporadic attempts at breathing. A subcutaneous Cardiazol injection of 1 c.c. improved respiration within 5 minutes and breathing was normal after $^1/_2$ hour. *Kieser* advocates the injection of 1 c.c. Cardiazol in asphyxia neonatorum after freeing the respiratory passages. In cases of *blue* asphyxia, the effect was, without exception, almost instantaneous. The first cry was heard after a few seconds and there was hardly ever occasion for the use of lobeline and artificial respiration. In cases of *white* asphyxia, where lobeline, insufflation, artificial respiration, etc. are the customary measures, the addition of Cardiazol produced a

stage, the power of the parturient woman is undoubtedly increased by Cardiazol, the pains showing greater constancy and the expulsion of the fœtus being accelerated. Also *Hüssy* writes that hypophyseal preparations can be combined with Cardiazol in the same manner as quinine in order to prevent a possible lessening of the fœtal heart-sounds.

According to *Bachner* it is worth while attempting to counter the diminution of the fœtal heart-sounds (change in fœtal circulation on fœtal head entering pelvis) by means of chloroform inhalation and Cardiazol. Also *Uter* is of opinion that subcutaneous or intravenous Cardiazol injections administered to the mother at that stage must have a beneficial effect on the fœtal circulation.

Obstetric operations

Sztehlo invariably administers 1 c.c. ephedrine + 1 c.c. Cardiazol after *Cæsarean section*. This medication has not only proved beneficial as a tonic for the maternal heart but also as an excitant of the fœtal circulation. From the time of the introduction of Cardiazol, now regularly employed, the infants are readily lifted from the uterus and, in most cases, begin to cry immediately. In premature extrusion of the placenta following uterine incision, *Vogt* gives intravenous continuous drop infusions of a 5% Calorose* solution with an addition of Cardiazol, Digipuratum (Knoll), strophanthin, etc., to assist blood transfusion.

Artificial abortion

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surprising and immediate improvement of the heart action, followed shortly after by breathing and reddening of the skin. In view of its remarkably rapid action, *Kieser* regards Cardiazol as superior to all other remedies.

Fecht advocates the following method of *Cardiazol injection into the umbilical vein* in the treatment of asphyxia neonatorum, a method which has proved very successful in the 31 cases described by him: immediately after detachment of the umbilical cord a thin venous cannula is inserted into the umbilical vein and $^1/_2$ to 1 c.c. Cardiazol injected after aspiration of a little blood. Blue-asphyctic infants quickly recovered after the Cardiazol injection and in more than half the cases the first cry was uttered already during injection. In about 40%, regular respiration commenced shortly after the injection in the warm bath. Silvester's respiration had to be resorted to only once. In white asphyxia, improvement and regularization of the cardiac action ensued in every case. As secondary remedies, lobeline, skin irritation and artificial respiration were used. *Nevinny* recommends intramuscular injections of Cardiazol together with skin stimulation, alternate hot and cold baths, in blue asphyxia of infants. In the still more dangerous white asphyxia, direct injection of Cardiazol and lobeline solution, diluted with physiological salt solution, into the umbilical vessels, is advised. In desperate cases intracardiac injection (adrenaline, Cardiazol, etc.) is advocated. Once the respiratory function is stimulated, the most careful watch and immobilization of the infant for a series of days are necessary. Cautious stimulation of respiration and circulation requires the administration of 3—5 drops Cardiazol per os at intervals of no great length. In given cases, the remedy may also be injected

intramuscularly in the same way as other analeptics. Ample subcutaneous infusions with Cardiazol-glucose also appear useful. Injection of lobeline + Cardiazol into the umbilical vein (apart from CO_2 and artificial respiration) is advocated also by *Schmid* for the treatment of asphyctic infants still showing a trace of cardiac activity.

III. Child-bed

Anæmia

Hammerschlag uses, amongst other remedies, intravenous injections of Cardiazol in the treatment of anæmia.

Puerperal fever

Adler advises special attention to the maintenance of the cardiac function in puerperal fever, stating that the use of Cardiazol is indicated ab initio, for instance, in persistent elevation of the temperature. *Spiegler* also counsels close attention to the heart in puerperal fever and the administration of Cardiazol and suchlike remedies. *Kustner* adds Cardiazol to the injection fluid where cardiac insufficiency accompanies puerperal fever. *Louros* also gives Cardiazol and Cardiazol-Ephedrine as additions to sepsis-antitoxin injections. *Friedemann* likewise adds Cardiazol, etc., to intravenous continuous drop-infusions in puerperal fever treatment. *Derichsweiler* mentions Cardiazol among the remedies given by him in puerperal pyæmia. *Stickel* recommends several daily intramuscular injections of camphorated oil or Cardiazol in acute failing of the cardiac function.

Lactation

Rosenblatt states that Cardiazol displays no action on the nursing breast.

PEDIATRICS

A. The prematurely born

According to *K. Schneider*, Cardiazol is extremely valuable in the treatment of prematurely born infants to abolish a variety of *states of debility*. *Moro* says that he has found Cardiazol efficient beyond expectation against the debility in prematurely born or congenitally feeble infants. *Nevinny* describes his favourable experience with Cardiazol-glucose infusions in the evolution of prematurely born children. Suitable compositions for infusions of this kind are sterile solutions of 4 gm. glucose, 0·07 gm. Cardiazol, 0·7 gm. sodium chloride and distilled water ad 100 c.c. Up to 100 c.c. can be injected through a single puncture. The infusions with Cardiazol as an addition are more uniformly absorbed. The *gain in weight makes regular progress also after the discontinuance* of the infusions. The improving action of Cardiazol on respiration and circulation persists likewise. The rousing action of Cardiazol, finally, is a welcome feature because it develops much greater vivacity and increases the appetite in somnolent infants. *Teebken* is another writer using Cardiazol in premature birth. *Maurer* begins the treatment of debilitated prematurely born infants with 2–4 drops of Cardiazol, given several times daily. A case of congenital debility (premature birth) successfully treated with Cardiazol is described by *Teruel Solana*. *Lust* administers analeptics such as Cardiazol in *cardiac dysfunction* of the prematurely born. *Finkelstein* as well as *Spiliopoulos* give lobeline or Cardiazol for the regularization of the respiration in congenital *asphyxia*. *Kollmann* saw a favourable effect from Cardiazol in a desperate

attack of asphyxia in a prematurely born infant, then 3 weeks old. The symptoms disappeared within 2 minutes after a subcutaneous injection.

B. *Alimentary disturbances*

(a) Diarrhœas

Dyspepsia

Manicatide includes Cardiazol among the remedies to be used in the treatment of dyspepsia in debilitated children. *Lust* advocates Cardiazol, etc., in dyspepsia to prevent collapse. *Spiliopoulos* gives subcutaneous injections, 2–4 times daily, of 20–40–80 c.c. physiological solution or 5% glucose solution with some analeptic added (e.g., $^1/_2$–1 c.c. Cardiazol with each injection) for the treatment of dyspepsia with vomiting. Intravenous injections of a 10–20% glucose solution in the same amounts, twice to thrice daily, with $^1/_2$ or 1 c.c. Cardiazol, have proved even more useful. The mixture may also be used for long-retained clysters. *v. Mettenheim* gives 3–5 drops of Cardiazol repeatedly in acute infantile diarrhœas to combat states of collapse. In *Klinke*'s opinion the use of analeptics is indispensable also in slight forms of diarrhœa for which reason he gives 5–6 drops Cardiazol every 3 hours to infants up to 3 months of age. *Filippi* prescribes Cardiazol (1 c.c. of a 5% solution, twice daily) in infantile summer diarrhœa, etc.

Toxicosis (alimentary intoxication)

De Rudder maintains that circulatory tonics (Cardiazol) are indispensable in grave forms of infantile diarrhœa, especially those

associated with intoxication. *Lages Netto* prescribes analeptics in serious forms of diarrhœa, e.g., 5–6 drops of Cardiazol every 3 hours. *Lust* advocates the administration of analeptics (at intervals of 2–3 hours) in toxicosis for the purpose of improving the circulation. Internally he gives Cardiazol, etc. In *Manicatide's* view camphor must be used with caution in the treatment of toxicosis with collapse, in view of the hepatic insufficiency which frequently accompanies these cases. He therefore gives the preference to Cardiazol (liquid). *Spiliopoulos* also uses analeptics in the treatment of toxicosis, either subcutaneously or intravenously in combination with glucose solution; of Cardiazol, for instance, $^1/_2$–1 c.c., once to twice daily. *Kollmann* gave Cardiazol in a case of alimentary intoxication to combat the circulatory insufficiency. *Dragišić* recommends Cardiazol in alimentary intoxications in the usual dosage (apart from caffeine). *Mertz* and *Eschbacher* were able completely to abolish the circulatory debility in a 5-months-old infant with enteral sepsis by the oral administration of 0·025 gm. Cardiazol. *Wiener* treats infantile intoxication with glucose infusions to which small doses of excitants (Cardiazol, etc.) are added. *Scheer* advocates daily subcutaneous infusions in *exsiccosis* until the loss in weight is arrested, and, in addition, liberal administration of heart and vascular remedies, e.g., Cardiazol (5–10 drops several times daily). If there is much vomiting he gives Sympatol* and Cardiazol alternately, subcutaneously in 0·5 c.c. doses and at intervals of 3–6 hours.

Gernsheim has given Cardiazol injections with much success in acute gastro-intestinal catarrhs, especially during the foodless period of 18–24 hours. The brilliant results obtained with Cardiazol in, often moribund, infants are largely ascribed by him to

the circulation-promoting property of the remedy. *Leitner* describes his treatment of grave cases of acute dyspepsia (20) and especially those associated with alimentary intoxication (6), in infants of 3–20 months of age. Subcutaneous injections of $^1/_2$–$^3/_4$ c.c. Cardiazol produced a slowing and strengthening of the pulse within 3–4 minutes so that stomach lavage could be performed without the risk of collapse. About 30–45 minutes after that operation another $^1/_2$–1 c.c. Cardiazol was administered. A protracted effect was obtained with Cardiazol liquid; likewise in gastric irritation, by the simultaneous injection of Cardiazol and camphorated oil, or Cardiazol injections given every 1–2 hours. The remedy also rendered good services in follicular enteritis where it was given in physiological solution. *Spiliopoulos* says that special attention must be paid to the tonicising of heart and circulation in gastro-intestinal infections as well as to the combating of dehydration. In this connection he uses intravenous injections of glucose solution to which an analeptic is added (20–40 c.c. 10% glucose solution + 1–2 c.c. Cardiazol, once or twice daily).

Schaffler mentions as the most important measure against threatening cardiac debility in summer diarrhœa, timely intravenous injection of glucose and excitants (i.a., Cardiazol). The remedy is also recommended by *Dragišić* in infantile summer diarrhœa at the beginning of the fasting period, to prevent collapse. He uses the remedy also as a preventive of collapse in toxicoses due to sunstroke.

Addendum: *Intestinal stenosis (infantile meteorism)*

Januschke had very good results with Cardiazol in 0 01 gm. doses in 20 cases of infantile meteorism, i.e., functional intestinal

stenosis impeding the expulsion of intestinal gases. The abdominal pains were quickly relieved and the gases expelled without difficulty.

(b) Nutritional disturbances

Dystrophy

In infantile dystrophy *Dabowsky* uses Cardiazol and similar substances to support the circulation.

Atrophy (decomposition)

Cardiazol is among the remedies recommended by *Kostić* in atrophy or dystrophy and severe diarrhœas (intoxication). *Mertz* and *Eschbacher* have used Cardiazol in atrophy and intoxication with grave states of collapse in infants. Subcutaneous injections of 0·5 c.c. Cardiazol resulted in excellent and no doubt life-saving effects. In an infant of 4 months of age who collapsed seriously twice during one night, no further collapse occurred after 4 oral doses of 0·05 gm. Cardiazol. *Koschate* describes the life-saving action of Cardiazol in an infant of 6 weeks of age which, through constant and uncontrollable vomiting and diarrhœa, had got into a state of grave atrophy and decomposition and showed no trace of respiratory or cardiac function. Within a few seconds after an intracardial injection of 3 (!) c.c. Cardiazol, the heart sounds were audible through the stethoscope. Subsequent cardiac massage maintained the cardiac activity with feeble but distinctly perceptible beats. Further treatment consisted in hourly administration of Cardiazol liquid and the child's life was saved. It is notable that no signs of convulsions were observed despite the large dose administered.

According to *Moro*, Cardiazol proved of great value also in infantile atrophy and *dysenteriform enteritis*. *Dragišić* also recommends Cardiazol as a preventive of collapse in infantile dysentery. *Spiliopoulos* stresses the necessity for analeptic measures against possible circulatory complications in dysenteric enterocolitis ($^1/_2$–1 c.c. Cardiazol intravenously, once to twice daily).

Addendum: *Diabetes*

Stolte advocates the addition of a Cardiazol injection to the insulin medication in infantile coma diabeticum in given circumstances. *Spiliopoulos* advises the administration, in coma diabeticum, of abundant liquid and of restoratives: caffeine or Cardiazol.

C. *Cardiac and Circulatory Disturbances*

Feer mentions Cardiazol among the analeptics with a stimulant action on the vasomotor and respiratory centres used by him in acute circulatory debility. *Lust* states his preference for Cardiazol (injected subcutaneously) among vasomotor excitants in the treatment of circulatory and cardiac insufficiency. In view of its rapid action on the respiratory centre, Cardiazol is regarded as the best of analeptics. It is *Bessau*'s impression that camphor is more and more ousted by Cardiazol as a circulatory stimulant, especially as it can also be given internally. According to *K. Schneider*'s experience, small doses of Cardiazol will prevent a deterioration of the cardiac function or improve existing circulatory debility in infants. Continued oral doses of Cardiazol gave

good results also in grave circulatory weakness, as in pneumonia or alimentary intoxication. In comparing Cardiazol with caffeine, he describes it as a special advantage possessed by the former that it produces no trace of psychomotor restlessness, an important point especially in pneumonia. *Rominger* recommends Cardiazol, etc., in the treatment of *collapse* in very young children and the same also in protracted states of vascular debility.

According to *Lust,* Cardiazol and similar preparations are often of greater service in acute cardiac debility with congestive symptoms than digitalis. Also *W. Schäfer* is of opinion that in acute failure of the cardiac function and the circulation in infancy, the real restoratives such as Cardiazol must be brought into service first of all. *Brdlik* gives Cardiazol and similar products in the place of camphor in cardiac insufficiency. Cardiazol can also be given in cases of hepatic insufficiency where the use of camphor inspires apprehension on account of its toxic action. *Hamburger* is among those using Cardiazol in acute cardiac debility. *Kleinschmidt* recommends it in acute endocarditis with manifestations of a failing heart. *Fischl* also employs Cardiazol in collapse due to acute endocarditis and *Teyschl* gives it against cardiac debility in endocarditis and myocarditis.

D. Diseases of the Respiratory Organs

(a) Bronchitis

Januschke's trials with Cardiazol in the treatment of acute and chronic bronchitis in a large number of children showed that the existing stenotic bruits disappeared or greatly diminished under the medication in a surprisingly short time.

(b) Bronchial asthma (bronchial stenosis)

Januschke also established the fact that Cardiazol, given subcutaneously, is able to abolish bronchial stenosis quickly and completely in certain forms of bronchial asthma (also in children).

(c) Glottic spasm

In glottic spasm, *Ibrahim* recommends an injection of camphor or Cardiazol against attacks of faintness.

Addendum: *Hypertrophy of the thymus gland*

Kollmann relates a case of asphyctic danger in a child suffering from hypertrophy of the thymus gland. After the injection of 1 ampoule of Cardiazol the alarming symptoms disappeared promptly.

(d) Bronchopneumonia, pneumonia

In *bronchopneumonia* of new-born infants with circulatory disturbances, *Hammerschlag* administers Cardiazol (among other remedies). Also *Kutter* recommends Cardiazol for the therapy of bronchopneumonia where cardiac and circulatory debility threatens. *Oxenius* is another writer recommending Cardiazol in such cases ($^1/_2$ ampoule every 4 hours, or Cardiazol liquid in 4 doses of 8 drops). *Bambouris* also preferably uses Cardiazol as a circulatory tonic since Cardiazol has a selective action on the respiratory and vasomotor centres resulting in a rapid abolition of dyspnœa and cyanosis. From the beginning of the illness he gives 5–10 drops every 3 hours until the patient is well. *Kollmann* gave Cardiazol more particularly in bronchopneumonia, partly subcutaneously and partly orally. A favourable effect on the circulation was clearly seen as quickly as 2–3 minutes after an injection and im-

good results also in grave circulatory weakness, as in pneumonia or alimentary intoxication. In comparing Cardiazol with caffeine, he describes it as a special advantage possessed by the former that it produces no trace of psychomotor restlessness, an important point especially in pneumonia. *Rominger* recommends Cardiazol, etc., in the treatment of *collapse* in very young children and the same also in protracted states of vascular debility.

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10 drops every 2–3 hours according to circumstances. *Dazzi* speaks of the use of Cardiazol in acute pulmonary diseases with circulatory debility in children between 1 and 6 years of age. He finds that the subcutaneous injection of the remedy produces a significant effect on the pathologically changed circulatory and respiratory functions. Lessened frequency and improvement in the quality of the pulse, through a rise in the maximal blood-pressure and elevation of the differential blood-pressure, and improvement in the respiration were most pronounced in the cases associated with grave hypotension. The maximum of effect was observed already after 5 minutes. The action on the circulation lasted over 2 hours. Noxious cumulative effects, toxic disturbances of any kind, states of irritation of the nervous system such as are occasionally met with after injection of camphor, have never been observed. The fact that a simple subcutaneous injection suffices to produce an extremely rapid and complete effect is regarded as a special advantage of Cardiazol, more particularly in infantile practice. *Gernsheim* has used Cardiazol mainly in affections of the respiratory organs, especially in bronchopneumonia and croupous pneumonia. He generally administers the remedy intramuscularly and has seen positively life-saving effects in many cases. He has come to the conclusion, therefore, that the best method of treatment is tonicization of the circulation with Cardiazol and plenty of fresh air, in addition to stimulation of respiration and expectoration. Where Cardiazol liquid was administered per os, relatively large doses were given (1/2 c.c., 4–5–8 times within 24 hours). *Leitner* reports 12 cases of croupous pneumonia in which the subcutaneous injection of 1 c.c. Cardiazol, night and morning, and internal administration of 6–10 drops, 3–4 times

provement in the respiration soon followed. According to *Marino*, Cardiazol supports the circulation in notable fashion in infantile bronchopneumonia (injected during the acute period and administered per os in the later stages). Moreover, the remedy has a favourable influence on respiration. *Schächter* looks upon Cardiazol as a powerful stimulant in infantile bronchopneumonia and *Tatka* regards it as particularly suited for the treatment of bronchitis and bronchopneumonia, especially in children to which latter it is invariably administered by him. Unusually easy expectoration in children after the administration of Cardiazol is mentioned as a striking feature. Respiration, superficial and irregular due to the high temperature, became easier and deeper. Where collapse threatened, Cardiazol promptly effected an improvement in the pulse quality. *Spiliopoulos* advises, in cases of bronchopneumonia, the intravenous injection of $^1/_2$ c.c. Cardiazol or caffeine, once, twice or thrice daily before packing.

Lust favours Cardiazol for the prevention of circulatory failure in *croupous pneumonia*. *Oxenius* uses Cardiazol in infantile pneumonia as one of the central vasomotor stimulants. *Wiskott* advocates the use of excitants, including Cardiazol, in pneumonia with a decompensated circulation. *Kochmann* gives Cardiazol in pneumonia (in drops); in acute collapse, Cardiazol + adrenaline. *Frick* refers to Cardiazol as the remedy of choice in infantile pneumonia saying that even infants can be given doses of 5–15 drops every 2–3 hours. *Kühl* prescribes Cardiazol, etc., in pneumonia (especially "blue" pneumonia) of infants and young children. The administration of analeptics in infantile pneumonia is recommended by *Reuss* where circulatory insufficiency threatens. He gives Cardiazol subcutaneously several times daily,

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daily, brought complete success. In 5 cases of *metapneumonic empyema*, Cardiazol was successfully added to the Optochin* medication ($^1/_2$–1 c.c. Cardiazol subcutaneously, 2–3 minutes before puncture or irrigation).

E. *Infectious Diseases*

(a) Measles

In measles exhibiting symptoms of *circulatory debility*, *De Rudder* prescribes Cardiazol, among other remedies. Cardiazol is also very efficacious in the treatment of *pneumonia complicating measles*. In cases of circulatory disturbances in measles, *Nassau* recommends the combination of antipyretics with caffeine, Cardiazol, etc. *Moro* states that subcutaneous or oral administration of Cardiazol enabled him to regularize the circulatory and respiratory functions in infants from 6 to 10 months of age suffering from measles complicated by bronchitis and bronchopneumonia. The medication also prevented or overcame states of collapse, facilitated expectoration and shortened the duration of the illness. *Walter* refers to a number of cases of circulatory debility during an epidemic of measles which gave him the opportunity to convince himself of the efficacy of Cardiazol as an analeptic. In infants and young children, the medicament proved both of prophylactic and abortive value in regard to states of debility. *Walter* describes how in one especially grave case (a child, 10 months of age), 7–8 c.c. Cardiazol *liquid* was given *during* one night. The measure saved the child's life. In *Walter*'s experience, heroic doses of Cardiazol are well able to save life also in infantile practice and secondary phenomena are not observed.

(b) Whooping-cough

In the treatment of pertussis, *Eisner* has on various occasions given Paracodin (Knoll) together with Cardiazol to support the circulation. *Frick* recommends the administration of $^1/_2$ c.c. Cardiazol in whooping-cough-pneumonia prior to the application of the mustard poultice.

(The combination-product "Cardiazol-Dicodid" has proved to be particularly suitable for whooping-cough treatment. For details see p. 203.)

(c) Diphtheria

Cardiazol is given by *Lust* to support the circulation in diphtheria. *Hecht* also administers Cardiazol, etc., in such cases. Where, in diphtheric circulatory insufficiency, there is the slightest suspicion of myocarditis, *M. Fischer* gives Cardiazol or similar substances at the earliest possible moment. *Kiss* also gives stimulants, including Cardiazol, as soon as there are any signs of circulatory debility in diphtheria. The timely administration of (i.a.) Cardiazol is also advocated by *Orel* so that circulatory debility may be prevented, especially in septicotoxic diphtheria. *Chiari* likewise advocates the administration of analeptics (i.a. Cardiazol) against the circulatory debility occasionally present in the beginning of diphtheric attacks. *Spiliopoulos* prescribes analeptics for the tonicization of the circulation in diphtheria (e.g., $^1/_2$–1 c.c. Cardiazol in 10–20 c.c. 10% glucose solution, 2–3 times daily). *Mertz* and *Eschbacher* gave oral doses of 0 05 gm. Cardiazol, 3 to 4 times daily, in a case of nasopharyngeal diphtheria and clearly diphtherically damaged heart in a boy, 8 years of age, with the result of striking improvement in the pulse quality, but in addition

also rapid regression of the cardiac dilatation and disappearance of the cardiac bruits, so that clinical restitutio ad integrum was accomplished within 14 days. According to *Burghard*, Cardiazol is an excellent circulatory tonic in cases of diphtheric laryngeal stenosis. *Hottinger* has given Cardiazol (among other remedies) in toxic diphtheria in addition to serum treatment. *Löhr* states that the intensive administration of vitamin C, Sympatol* and Cardiazol, has rendered him valuable services in grave vascular paralysis accompanying diphtheria (as well as pneumonia).

Manicatide prescribes Cardiazol along with other medicaments to raise the blood-pressure in *collapse (serum disease)*.

Cardiazol is given by *Hecht* in 3 daily doses of 10 drops in *post-diphtheric circulatory irregularity* and the remedy was also used by *Choremis* in a case of post-diphtheric myocarditis.

(d) Scarlatina

Franck gives subcutaneous injections of 1 c.c. Cardiazol in scarlatina with a feeble pulse before administering scarlatina streptococcus serum and uses the remedy also in cardiac weakness. *Seyfardt* advises close observation of the behaviour of the heart and the injection of caffeine and camphor or Cardiazol against manifestations of cardiac debility. *Damskis* reports that in scarlatina he has had the best results with Cardiazol (liquid). The preparation has also been used by *Esser* and *B. Kraus* as a circulatory tonic and to combat acute myocarditis and endocarditis in scarlatina cases.

(e) Meningitis

Kollmann relates the case of an infant of 6 months of age suffering from epidemic meningitis; patient fell into a collapse-

like state twice on the occasion of a lumbar puncture and the subsequent injection of serum. 1 c.c. Cardiazol was administered 7 times, at intervals of 1 hour, after which definite improvement was established. According to *Leitner*, acute meningitis and hydrocephalus are likewise indications for Cardiazol. Since he has used the remedy prior to lumbar punctures he has had no further cases of collapse. Also *Ibrahim* recommends analeptics, including Cardiazol, in meningitis where restorative measures are required. *Glanzmann* and *Heller* advocate the administration of caffeine or Cardiazol in asphyctic suppurative meningitis in children, to prevent collapse.

(f) Influenza

In influenzal affections in very young children, *Putzig* obtained the best results with Cardiazol, given intramuscularly in 0·2–0·5 c.c. doses. *E. Müller* is in favour of Cardiazol in 3 or 4 daily doses of 5–10–15 drops, where circulatory disturbances occupy the foreground in acute influenza. Cardiazol is one of the medicaments prescribed by *Gaupp* as a circulatory stimulant in the treatment of influenzal lung complications. *Sindler* reports good results from Cardiazol in the treatment of infants suffering from bronchopneumonia complicating influenza. He states that the extremely mild convulsive action of Cardiazol renders the preparation particularly useful in the treatment of young children. He cites the case of an infant in a state of heightened spasmophilia in which 6 c.c. Cardiazol, injected in the space of 24 hours, produced no notable reaction.

(Cardiazol-Quinine in the treatment and prophylaxis of influenza is discussed on page 168.)

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Addendum: *Phlegmons*

Kollmann relates a case with extensive phlegmons in which he used Cardiazol to prevent circulatory debility.

(k) Syphilis (congenital)

In the fever therapy of congenital syphilis, *Soeken* favours Cardiazol in particular. He says that with this medication circulatory complications are a thing of the past.

F. Tetany (Spasmophilia), Eclampsia

Cardiazol in liberal doses figures amongst the remedies used by *Lust* in *spasmophilia (tetany)* for the purpose of circulatory stimulation. *Zappert* is of opinion that in infantile spasms (e.g., terminal spasms) the treatment of the convulsions is of less importance than that of the circulatory damage. In this connection he recommends Cardiazol (among various remedies). *Longo* reports a case of serious convulsions with unconsciousness in which Cardiazol proved very successful. Cardiazol, etc., are also used by *Filippi* in the treatment of infantile convulsions.

Pascarelli speaks of good results in various cases of *convulsions* with high temperature, tachycardia, dyspnœa and somnolence in their train, which precede many infectious diseases. In these, Cardiazol rendered him satisfactory services.

According to *Leitner*, Cardiazol is an excellent remedy in *eclamptic crises* and, above all, in status eclampticus. In these cases he always injects the Cardiazol in $^1/_2$ c.c. doses, together with sodium phenobarbitone.

(g) Typhus abdominalis, dysentery

Spiliopoulos is of opinion that the use of analeptics, e.g., Cardiazol, is necessary in typhus abdominalis (in mild cases, 5 to 15 drops Cardiazol every 3 hours; in more severe cases, intravenous injections of $1/2$–1–2 c.c. in 5–10% glucose solution, twice to thrice daily). The administration of Cardiazol (or similar substances), in liquid form or by injection, is also advocated by *Rocha* in the treatment of typhoid fever in children (before the bath). *Bischoff* is likewise of opinion that cardiacs and circulatory tonics, including Cardiazol, are imperative in the therapy of typhus abdominalis and dysentery.

(h) Malaria

Where there are signs of circulatory debility in malaria-infected children, *Laurinsich* gives Cardiazol, etc. *Weselko* has likewise had very good results with Cardiazol in malaria. He instances the case of a girl of 7 years of age with tonic-clonic spasms and deep unconsciousness. Injections of Cardiazol abolished the spastic condition and restored patient to consciousness.

(i) Sepsis

To support the circulation in sepsis, *Lust* injects tonic agents such as Cardiazol subcutaneously several times daily. *Finkelstein* also points out the necessity of paying incessant attention to the maintenance of the circulation, mentioning Cardiazol among the remedies answering that purpose. *Fischl* has used Cardiazol successfully in septic infections of the newborn and infants. *Teyschl* also recommends substances such as Cardiazol to maintain the circulation in sepsis neonatorum. *Hammerschlag* is in favour of its use in the treatment of umbilical infection in the newborn.

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(b) Asthma cerebrale

For the treatment of cerebral asthma, *v. Romberg* advocates injections of Cardiazol plus morphine or similar narcotics, at the height of the attack.

(c) Cerebral hæmorrhages, cerebral embolism and traumata, comatose states

In circulatory debility due to *cerebral hæmorrhages*, *Fleischmann* injects Cardiazol or similar substances.

Bing advocates remedies such as Cardiazol in *cerebral embolism* or *cerebral thrombosis*.

In *commotio*, *Nehrkorn* stimulates the circulatory action by injections of Cardiazol, etc.; *Bing* employs the same treatment in syncope and concussion of the brain; *Fleischmann* uses it in *traumatic brain lesions*.

Hitzenberger counsels an immediate intensive circulatory therapy in every case of *coma*, recommending Cardiazol and certain other substances for the purpose. Also *Fleischmann* recommends Cardiazol, etc., as a circulatory tonic in comatose conditions (especially coma diabeticum).

("Coma diabeticum" is discussed in greater detail on page 89.)

(d) Paralysis agitans (Parkinsonism)

Against congestions (flush), palpitations, vertigo, occurring during atropine treatment of Parkinsonism, *Römer* gives Cardiazol, or Cardiazol-Ephedrine, in addition to tincture of valerian. *Roasenda* complements the scopolamine-atropine treatment by giving 15 drops of Cardiazol twice to thrice daily as a circulatory tonic, and recommends this method.

NEUROLOGY AND PSYCHIATRY

A. Neurology

I. Diseases of the Peripheral Nerves

Neuralgias (Trigeminal neuralgia)

In disturbances during pyrexial treatment of trigeminal neuralgia, *Böckheler* makes use of circulatory tonics, regularly given on fever days, among them Cardiazol, administered by subcutaneous injection.

II. Diseases of the Medulla and Medulla oblongata

(a) Tabes dorsalis

In cases of gastric crises associated with circulatory disturbances, *Mattirolo* advocates the administration of analeptics, including Cardiazol.

(b) Multiple sclerosis

Dreyfus and *Hanau* also give circulatory tonics, e.g., Cardiazol, during pyrexial treatment (especially malarial therapy) of multiple sclerosis.

(c) Bulbar paralysis, Landry's paralysis

In acute bulbar paralysis, *Mattirolo* gives analeptics, i.a., Cardiazol, to support the circulation, and the same in acute Landry's paralysis.

III. Diseases of the Brain

(a) Meningitis

Injections of Cardiazol, etc., are recommended by *Fleischmann* in meningitis, before or during the bath.

(b) Asthma cerebrale

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(e) Neurosyphilis

Kirschbaum administers Cardiazol during *pyrexial treatment of metasyphilis.* He has frequently succeeded in reviving patients who collapsed unexpectedly during acme, within a few minutes, by giving them 2 injections of Cardiazol (of 1–2 c.c.). The injections were then repeated at intervals of 1–2 hours and tided patients safely over the critical day on which either the quinine treatment had to be begun, or it was even possible to continue pyrexial treatment for several more days with the support of Cardiazol. *Kirschbaum* recommends 1–2 prophylactic injections of Cardiazol during the rigors of the last few pyrexia days, saying that these have always proved of value. Even high doses of Cardiazol have not been known to produce untoward effects. Much good has frequently been seen also from the oral administration of Cardiazol in combination with digitalis. *Kumbruch* recommends doses of caffeine, in given cases in combination with Cardiazol, in pyrexial treatment of syphilitic nerve diseases. He says that this precautionary measure has always prevented undesirable incidents.

Addendum: *Craniectomy*

Monteiro describes the excellent results obtained by him in the preparatory drug treatment of his craniectomy patients. He commences with the administration of calcium chloride, sodium bicarbonate and hexamethylentetramine 4 days before the operation. On the 2 last days ventricular punctures are performed following injections of Cardiazol. Before the chisel is used, 1 ampoule of Cardiazol is injected intravenously whilst 1 ampoule of Cardia-

zol-Ephedrine is given by the subcutaneous route. Cardiazol is continued also after operation as a circulatory tonic and respiratory stimulant.

B. Psychiatry

I. Psychoses

Alcoholism (see p. 76).

Morphinism, etc. (see p. 77).

II. Progressive Paralysis

The administration of cardiacs and analeptics, i.a. Cardiazol, during the fever attacks in *malarial therapy* of paralysis, and, where needed also during intermission, is recommended by *Wagner-Jauregg*. Also *Herschmann* gives Cardiazol apart from Digipuratum (Knoll) on pyrexia days in malarial therapy of progressive paralysis. *Pilcz* includes Cardiazol among the remedies used by him for the treatment of the circulation during malarial therapy of paralysis. *Kähler* gives 15 drops Cardiazol thrice daily from the first day of inoculation, or from the onset of the first prodromal rise in the temperature. Alternatively he gives 15 drops of strophanthus tincture per os and with either method has never had a death due to heart failure. Cardiazol enabled *Schönmehl* to remedy circulatory disturbances arising during malarial treatment, and speedily to combat conditions of collapse. The average dosage amounted to 15–20 drops Cardiazol liquid, thrice daily, both whilst the treatment lasted and during 8–10 days thereafter. During rises and falls in the temperature 1 ampoule of Cardiazol was injected subcutaneously each time. *Schönmehl* declares that

Cardiazol is indispensable in malarial therapy. *Trautmann*, who has great experience of malarial therapy, is of opinion that the circulation requires careful observation and regularization from the moment of inoculation. Cardiazol has proved to be the best tonicising agent during the fever period. This treatment should be commenced prophylactically at the onset of the first attacks of fever with the administration of 20 drops Cardiazol liquid, 3 times daily (as long as the tertian type is maintained, the same medication also on afebrile days). Where collapse occurs unexpectedly, a combination of Cardiazol with caffeine, lobeline, in certain cases also strychnine, or an intravenous injection of 20 c.c. of a 40% glucose solution to which 1 c.c. Cardiazol and 0·2 mgm. strophanthin are added, is to be recommended. With the last-mentioned combination, Cardiazol is of additional importance because it enables the reduction of the strophanthin dose to a minimum. When the state of collapse is overcome, further doses of Cardiazol (1 ampoule every hour) keep the pulse strong and steady. Cardiazol is also used by *Kolkmann* as an efficient circulatory tonic during malarial treatment. *O. L. Weiss* says that the Cardiazol medication should be employed during the entire course of malarial therapy and also during the subsequent period of apyrexia. *Mondio* describes a case of paralysis treated by malarial therapy in which the influence of Cardiazol was found most useful. *Weygandt* is in favour of X-ray examination of the heart and large vessels before malarial therapy of progressive paralysis is begun. In his experience, 50% of all metasyphilitics have some defect of the heart or aorta. (Mesaortitis syphilitica appears to be particularly dangerous.) *Weygandt* therefore recommends careful observation of the circulation and the use of Cardiazol, etc.

Hinrichs has given Cardiazol, in tablet form, in various cases of progressive paralysis treated by *relapsing fever*. During the fever days he gave 2 tablets daily and an additional tablet where the temperature fell critically. With this medication, patients have been able to tolerate falls in the temperature up to nearly 4° C. without untoward occurrences and with an always satisfactory pulse, no other remedies having had to be resorted to.

Siemerling combats circulatory debility, occurring during *pyrexial therapy* of progressive paralysis and tabes, with Cardiazol, etc.

III. Schizophrenia

In the convulsion therapy of schizophrenia, *v. Meduna*[1] tried intravenous injections of Cardiazol in the place of the previously used camphorated oil. Cardiazol proved an excellent agent with which to provoke epileptiform attacks. The initial dose given in every case was 5 c.c. (0 5 gm.). Where the convulsive reaction failed to take place, the dose was increased by 1 c.c. Cardiazol (0·1 gm.) with each further injection until the classical epileptic attack occurred. The injections were given twice weekly. The largest total dose ever required was 10 c.c. (= 1 gm. Cardiazol)†. Among the 101

† From the practical point of view, *v. Meduna's*[3] findings concerning the influence of the *speed of the injections* are of the utmost importance. Whereas 1 c.c. Cardiazol injected in the space of a second showed the minimal convulsive dose to be x gm Cardiazol, the same quantity x, injected intravenously in twice that time (that is, at a speed of 1/2 c c. within a second), failed to produce convulsions in some of the patients Where the established convulsive dose was given in fractions at intervals of 10—15 seconds, no convulsions ensued. Thus is the convulsive effect geometrically proportionate to the speed of injection (see p 36) and it is evident that to produce

patients treated by *v. Meduna*, 41 (40%) experienced complete remission. In some, the purpose was achieved after 4–5 attacks, in others only after 18–20. If 20 epileptic attacks are unsuccessful it is useless to continue the treatment. *v. Meduna*[2] also reports that with the convulsion therapy of schizophrenia as introduced by him, the most conscientious physiological, röntgenological or electrocardiographic control of the heart never revealed damage to the latter, not even in cases where numerous injections of large doses of Cardiazol had been necessary (1 patient, for instance, received 53 injections of 5–10 c.c. Cardiazol, and went through 33 epileptic attacks). *v. Meduna* has given more than 2000 injections in supertherapeutic doses and has provoked over 1000 epileptiform attacks, none of which was accompanied by any notable complication. He himself writes: "Thus may the Cardiazol therapy (viz. *convulsion* therapy) be regarded as completely harmless." The one contraindication in his opinion are organic heart disorders or acute febrile diseases. The percentage of cured cases in progressive (not permanently established) schizophrenia was 82. In regard to the age of the disorder, it has been shown that the *cases subjected to treatment within 6 months from the first* manifestation of the disease, have an 80–90% prospect of cure. Where the disorder is of more than a year's standing that prospect is very greatly diminished. Cases of more than 4 years' standing have practically no prospect of cure. *Krüger* found that 3 c.c.

convulsions, Cardiazol must reach the nerve centres in high concentration This is probably the reason why *v. Meduna* required a Cardiazol dose greater by 3–5 c.c. for intramuscular injection. If these significant findings apply already to maximum "supertherapeutic" doses, then they apply all the more to therapeutic doses The latter can, according to *v. Meduna*, be repeated in suitable amounts at suitable intervals without risk of cumulation or attacks of a spastic nature

Cardiazol was generally sufficient; in some cases even lower doses ($1^{1}/_{2}$–3 c.c.) proved adequate. The susceptibility of schizophrenic and epileptic patients appears to be the same. Rapid injections of the same dose may provoke convulsions which slow injections fail to produce. Incidents or harmful effects from Cardiazol were not observed. *Schönmehl* used Cardiazol successfully also to break psychic stupor. He found, moreover, that the amount of Cardiazol found necessary to provoke epileptiform convulsions is a very valuable diagnostic aid: the convulsive dose for normal, healthy, persons is about 10 c.c.; for schizophrenic patients (according to *v. Meduna*), 5–7 c.c. Convulsions arising after the latter dosage and still smaller doses ($^{1}/_{2}$–3 c.c.) point to spasmophilia which must have pathological causes. *Wahlmann*'s observations in connection with convulsion therapy of psychoses are of interest. He had cases of catatonia, dementia paranoides, hebephrenia and manic-depressive insanity in 85% of which 5 c.c. Cardiazol provoked convulsions promptly. No noxious effects have been seen. The injections were given to patients whilst in the fasting state, 1 c.c. Cardiazol being administered per 10 seconds. 5 out of 9 catatonia cases were not influenced. In hebephrenia the treatment made no perceptible impression. In one of three cases of dementia paranoides there was considerable improvement. In one case of manic-depressive insanity, with occasionally marked catatonic symptoms, sudden improvement occurred after 3 injections. *Wahlmann* mentions that his publication is intended to stimulate further research in this field. Also *Stuchlik* tried the Cardiazol convulsion therapy in catatonia, schizophrenia, states of amentia and for the breaking of neurotic tendencies (functional anuria). According to present experience chronic catatonic stupor is not

liable to be favourably influenced but the results are better in recent stuporous conditions. In some forms of amentia the effect was superior to that seen from other therapies.

IV. Epilepsy

Popea, Eustatziu and *Ionescu* find that *status epilepticus* runs a milder and shorter course in patients treated with Cardiazol (1 tablet or 20 drops every hour); also the twilight state after attacks is briefer and less profound.

Differential diagnosis of epilepsy:

Langelüddeke, on the strength of his investigations, has reached the following conclusions respecting the diagnostic significance of experimentally provoked convulsions: (1) The rapid intravenous injection of 5 c.c. Cardiazol will produce convulsions in a large number of patients suffering from organic brain disorder, epilepsy or schizophrenia. (2) The course of the Cardiazol convulsions in epileptics corresponds entirely to the course of spontaneous convulsions. It follows that the Cardiazol convulsions represent a useful differential diagnostic guide as to whether a case is one of genuine or of symptomatic epilepsy. The use of Cardiazol injections as an aid to diagnosis in epilepsy is declared to be of general value also by *Stuchlík* who says that 3 c.c. was invariably sufficient to provoke an attack in an epileptic. *R. Stern* also recommends the slow injection of 2 c.c. Cardiazol into the brachial vein for differential diagnostic purposes in epilepsy stating that in none of dozens of cases the same dose of Cardiazol, injected intravenously, produced the slightest trace of a convulsive effect.

Schilling, on the other hand, thinks that far-reaching differential-diagnostic conclusions should not be drawn from convulsions provoked by intravenous Cardiazol injections alone.

V. Manias, melancholias, manic-depressive insanity

Wuth[1] recommends the administration of analeptics, including Cardiazol, in states of *manic excitation*.

In *melancholic depression* associated with circulatory debility, the combination of Dicodid (Knoll) with Cardiazol has, according to *Bufe*, proved "an inestimable gain", especially where patients were apathetic, lethargic or abulic. In a schematic plan of dosage, *Bufe* prescribes 1 tablet of 0·005 gm. Dicodid (Knoll), thrice daily to start with, for severe cases, the dosage to be increased every third day until 6 tablets are given thrice daily, whereafter the dosage is similarly reduced again. The daily dose of Cardiazol remains the same throughout and amounts to 1 tablet, thrice daily. With patients refusing oral medicaments, Dicodid (Knoll) ampoules and Cardiazol ampoules should be considered. Slighter forms of mental derangement can be usefully treated with Cardiazol-Dicodid Drops, 15 drops, thrice daily, rising to 45 drops, thrice daily.

Cardiazol is amongst the remedies enumerated by *Wuth*[2] as useful stimulants of the circulation in *manic-depressive insanity*.

VI. Neurasthenia (psychasthenia)

Licci has used Cardiazol, among other drugs, in nervous conditions of exhaustion, depressions and organic debility in *psychasthenics*.

Steck recommends the use of Cardiazol, etc., in addition to digitalis in the treatment of *delirium tremens* where indicated.

Cimbal has tried Cardiazol as a tonic for "nervy" persons and especially in cases of *nervous circulatory atony.* On the strength of his experiences Cardiazol impresses him as the most important remedial agent in neuropathies of that description, apart from digitalis. The action of Cardiazol is extremely favourable in children with circulatory depression habitus; more particularly also in asthenic infantile gigantism where the change in the circulation during the years of puberty fails to take place (i.e., the pulse amplitude during puberty retains its infantile habitus). Still more important is the Cardiazol medication in the forms of circulatory atony accompanying exhaustion dementia (amentia, delirium acutum, etc.). Cardiazol has also proved beneficial in hormonal deficiencies of the late and post-climacteric as well as in neurotic states of debility after infectious diseases (fatigue neuroses after diphtheria, influenza, kidney disorders and articular rheumatism). In these forms of neuropathy *Cimbal* gives 2–3 c.c. Cardiazol to tonicize the circulation and is of opinion that states of circulatory debility of many years' standing, seen in the congestion of all organs, can be slowly overcome by the improved perfusion engendered by Cardiazol. In cases of serious renal damage he has often observed a reduction of the nephrogenous hypertension and a simultaneous improvement in the amplitude after systematic Cardiazol treatment, persisted in for many months.

(See also *Cardiac neuroses*, p. 57.)

Addendum: *Artificial continuous sleep and "twilight sleep" therapy*

Hinrichs has given subcutaneous injections of Cardiazol in transient cardiac debility occurring during prolonged scopolamine-paraldehyde sleep, as well as in two cases of very grave collapse following a single dose of scopolamine-paraldehyde administered during the previous evening, the collapse being apparently due to intoxication. Shortly after each Cardiazol injection the circulation showed clear signs of stimulation, generally after 2–5 minutes. In cases of continuous sleep treatment (Somnifen*), *Salm* injects 1/2–1 c.c. Cardiazol simultaneously with the hypnotic. *O.L.Weiss* found that an intramuscular injection of 1 c.c. Cardiazol nearly always sufficed to interrupt normal "twilight sleep" where induced by the customary doses of Rectidon*, and to keep patients awake for about 1/2 an hour, chiefly for the purpose of administering nourishment. In many cases a dose of 30 drops Cardiazol answered the same purpose. The preparation is also a reliable antidote in Rectidon*-overdosage. It normalizes the circulatory and respiratory functions very quickly also where the state of the patient has an alarming aspect. The effect of an intramuscular injection is quite as reliable as that of an intravenous injection. *H. Fischer* has also used Cardiazol to interrupt therapeutic "twilight sleep" (hyoscine-morphine or Luminal*). 3 c.c. proved sufficient as a rule. In a few exceptional cases 6 c.c., in one case 9 c.c., was given intramuscularly. The colour of the skin always changed shortly after the injection owing to better perfusion; respiration deepened and sleep grew less profound. Patients awoke after about 10–15 minutes. No advantage was found to attach to intravenous administration as compared with intramuscular injection.

Cardiazol is thus able to rouse patients for a brief space of time during which they can be fed. Incidents, which arose in only 3 cases during induction of the narcotic sleep (hypersensitiveness to hyoscine-morphine and, in 2 instances, signs of collapse due to preceding agitation) were easily combated with Cardiazol. The margin of safety in the case of Cardiazol is relatively great so that the question of overdosage need hardly enter into consideration.

Hypnosis

According to *Hoff*, hypnotized patients can be awakened by Cardiazol.

UROLOGY

Catheter-fever

Boeminghaus recommends intramuscular injections of 2 c.c. or, in alarming conditions, intravenous injections of 1 c.c., in catheter-fever accompanied by marked circulatory insufficiency.

Urethroscopy

Americo Valerio reports good results from Cardiazol as a hæmostatic (urethroscopy, vaginal examination).

Functional anuria

Stuchlik had 2 cases of functional anuria in which the intravenous injection of 5 c.c. Cardiazol invariably provoked an epileptic attack with evacuation of the bladder.

Prostatectomy

Mollá names Cardiazol as one of the preparations used by him in premedication of prostatectomy cases.

DERMATOLOGY AND VENEROLOGY

Syphilis (and Gonorrhœa)

Ullmann recommends the use of (i.a.) Cardiazol to combat *vasoneurotic crises* in syphilis.

B. Kraus has employed Cardiazol very largely (425 cases) in arsenic therapy of syphilis as a *prophylactic against nitritoid crises.*

According to *Strauch*, cardiac perfusion must be improved by digitalis or Sympatol*, Cardiazol, etc., before specific treatment is instituted in *syphilitic aortitis* and *aortic insufficiency* with impeded coronary circulation.

Janson had good results from the intravenous administration of Cardiazol in the case of a woman who collapsed during pyrexial gonorrhœa treatment.

Gold therapy

By way of experiment *Paldrock* injected 1 Cardiazol ampoule subcutaneously 10 minutes before injecting gold. This enabled him to prevent secondary effects in all his cases. It is his rule now never to inject sensitive patients with gold excepting after prophylactic injections of Cardiazol.

Obliteration of varicose veins

Loben says that a Cardiazol syringe should be ready at hand before obliteration treatment of varicose veins is begun.

OTORHINOLARYNGOLOGY

Otitic sepsis

Denker and *Albrecht* advocate the use of circulatory tonics such as Cardiazol in the treatment of otitic sepsis.

Otosclerosis

In otosclerosis with symptoms of vasoneurosis, *C. Stein* was able to obtain a better influence on the ear trouble by the use of vascular stimulants (Cardiazol, etc.) than that of sedatives.

ODONTOLOGY

A. Collapse and similar incidents

Guttmann describes two serious cases of collapse in which the injection of 1 c.c. Cardiazol very rapidly effected improvement of the pulse and disappearance of the accompanying symptoms. Also *Grabner* administered Cardiazol with success in the treatment of collapse, shock, superficial or arrested respiration. *Dietrich* reports that Cardiazol proved of great value in an alarming attack of acute cardiac insufficiency experienced by an elderly lady during dental treatment. He describes the effect as positively life-saving. *R. Neumann* also says that Cardiazol should be kept at hand in ampoules for subcutaneous injection, or in solution for oral use (8—10 drops to $^1/_2$ tumblerful of water), for the treatment of untoward incidents (collapse).

B. Prophylactic use

Patients with labile hearts or a feeble pulse are, by *Guttmann*, given a Cardiazol tablet combined with 2 Bromural (Knoll) tablets or 1 Veronal* tablet, prophylactically, 20 minutes before induction of local anæsthesia. *Greiffenhagen* is likewise in the habit of giving Cardiazol prophylactically. He refers to more than 100 cases in which he gave 20 drops, or 1 tablet, 7—10 minutes before local anæsthesia, extractions, surgical measures as well as dentine anæsthesia. Since he has used the preparation he has had no disturbing secondary effects from injection anæsthesia except once in the case of a cachectic woman on whom he was unable to operate despite Cardiazol treatment. The rule is a good and normal pulse, normal respiration, quieting or total disappearance of agitation. *Dietrich* relates his favourable experience with Cardiazol in over 100 cases. He gave it in doses of 20 drops, or 1 tablet, in warm tea, for the prevention of expected fainting attacks. In the majority of cases the surgical operation was able to be performed after 10 minutes without further risk of faintness. On the strength of his experience he recommends the use of Cardiazol, especially for prophylactic purposes, before deep mandibular and dentine anæsthesias and, generally speaking, for the treatment of all frightened, feeble patients and those justifying the suspicion of possible collapse. To the latter group he gives Cardiazol whilst still in the waiting-room. *Grabner* has also used Cardiazol prophylactically. Difficult extractions and operations on the jaws were greatly facilitated thereby. *Grabner* gives Cardiazol to patients with labile habitus, even where it is a question of a simple extraction, a few minutes before the anæsthetic is injected. Occasionally he administers

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may also be doubled if required. Cardiazol may also be used for protracted treatment; several doses of 0·1 gm. daily.

The preparation can also be "dispensed" in its powder form, and in combination with other remedies, according to indications.

Children: Infants are given 0·05 gm. Cardiazol powder, $^1/_2$ tablet or $^1/_2$ c.c. Cardiazol liquid (= about 10 drops), several times daily, according to the necessities of a case. The dose for older children is 0·1 gm. Cardiazol powder, or 1 tablet, or 20 drops liquid.

The Cardiazol tablets should not be swallowed whole. They are best disintegrated in some liquid.

Cardiazol liquid is taken with a little water.

After oral administration the action of Cardiazol is much more persistent than after injection. In cases of lesser urgency the use of the tablets or the liquid form may, therefore, be recommended.

Injections

Cardiazol is injected subcutaneously, intramuscularly, intravenously or intracardially. The same ampoule preparation serves for every one of these methods and is also suitable for the mixed syringe (with strophanthin, Digipuratum [Knoll], Dilaudid [Knoll], etc.). The advantage of the *one* ampoule is the exclusion of confusion whilst the possibility of combining the ampoule contents with other preparations gives the physician every opportunity for individual treatment.

Owing to its exceptionally great solubility in water and lipoids the preparation is so rapidly absorbed that the action of a subcutaneous injection manifests itself almost as quickly as that

Cardiazol in the customary dose together with a Bromural (Knoll) tablet or a Neodorm (Knoll) dragée. Frightened patients are quickly reassured so that anæsthesia and operation take a normal course. Incidents, previously of frequent occurrence, have become very rare. *E. Schneider* also reports good results from Cardiazol as a prophylactic before local anæsthesia.

C. Post-Anæsthetic Phenomena

Dietrich says that after *ether*, *ethyl chloride* and *ethyl bromide narcoses*, a dose of Cardiazol quickly abolishes the symptom complex of nausea as far as manifested in a tendency to vomiting and numbness in the head. Patients recover from these symptoms more rapidly than without Cardiazol and can therefore be taken from the operating theatre with less delay. Also *Grabner* describes the favourable effect of Cardiazol after ether and ethyl chloride narcoses. Nausea and numbness disappear promptly and patients' condition improves visibly.

Reuber uses Cardiazol in the treatment of somnolence after Evipan-Sodium* anæsthesia. He gives his patients an injection of 1 c.c. when they awake; this enables him to eliminate all post-narcotic effects.

DOSAGE

Oral application

Adults: The average dose for adults is 1 tablet of 0·1 gm. or 1 c.c. (about 20 drops) of Cardiazol liquid, 3–4 times daily. Where necessary, this dose can be repeated every hour and it

and to shorten the post-narcotic sleep. Also in serious poisoning by hypnotics, opiates, etc., 1–2 of the 3 c.c. ampoules are injected intravenously or intramuscularly. The best effect is obtained by the administration of 2–3 c.c. intravenously and 3–5 c.c. intramuscularly. The intravenous injection should, generally speaking, be performed *slowly*.

Cardiazol ampoules of 5 c.c. are used in the convulsion therapy of schizophrenia (according to *v. Meduna*). Epileptiform attacks are provoked by the rapid intravenous injection of 5 c.c., or more, if necessary.

Children: The average dosage for infants is $^1/_4$–$^1/_2$ ampoule or $^1/_4$–$^1/_2$ c.c. of the 10% sterile solution. Older children receive $^1/_2$–1 ampoule. If necessary these doses may be repeated several times daily.

Rectal application

Cardiazol can also be administered rectally in the form of *suppositories*. The latter are not on the market but are prepared by the chemist:

R Cardiazol... 0·1 (–0 2) gm.
Ol. Cacao ..... ad 2 0 gm.
(D. tal. suppos. No. VI).

Cardiazol liquid can also be used in *microclysters*. 1–2 c.c. is added to about 10 c.c. water and the mixture injected with a glycerine syringe.

of an intravenous injection. Application through a vein will therefore only rarely have to be resorted to. The absence of irritant effects from subcutaneous injections merits emphasis. Infiltrates and necrosis at the site of injection do not occur.

There have been occasional complaints in the past that subcutaneous Cardiazol injections do not, in the case of sensitive patients, pass off quite painlessly. The Cardiazol ampoules have, *therefore, been adjusted by the addition of sodium phosphate*† to a hydrogen-ion concentration $p_H = 7{\cdot}5$ to 8; all sensation of pain is thereby practically eliminated. The Cardiazol ampoules are sterile and have unlimited keeping qualities.

Sterile Cardiazol solutions for injection can also be prepared by the chemist, according to individual prescriptions.

Adults: 1 c.c. of the sterile solution (0·1 gm. Cardiazol) is injected subcutaneously, intramuscularly or intravenously, according to the requirements of a case; every $^1/_2$–1 hour if necessary. In urgent cases, 2 c.c. may be injected. In alarming states of *collapse or respiratory disturbance, Cardiazol must be injected* every 10–20–30 minutes.

Cardiazol is also suitable to be added to *continuous intravenous drop-infusions* (e.g., 2 c.c. Cardiazol to 200 c.c. of a 10% glucose solution; rate of infusion = 1 drop every 1–2 seconds). The size of the Cardiazol addition, concentration of glucose solution, time of injection and rate of drop-infusion, depend on the severity of individual cases.

Cardiazol ampoules of 3 c.c. are used to rouse patients from narcosis in cases of overdosage of an injection- or rectal anæsthetic

† Di-sodium hydrogen phosphate, Na_2HPO_4, $12\,H_2O$

CARDIAZOL-QUININE

Heightening of quinine tolerance, acceleration of the quinine action, non-straining of circulation

PROPERTIES

The purpose of the combination is to *eliminate the secondary effects of quinine*, especially liable to occur with prolonged use and showing in circulatory and respiratory disturbances; but, above all, the action of Cardiazol complements that of quinine in all those fields of indication which demand a *support of the circulation*.

The solubility of the quinine salts is considerably increased by the Cardiazol addition. By means of the Cardiazol-Quinine ampoules it is possible to introduce relatively large doses of quinine in *pure aqueous solution* (without the addition of urethane, etc.) into the organism. The slight viscosity of the solution ensures perfect tolerance of the injection, apart from rapid absorption and consequent *acceleration of action*.

The investigations carried out by *Flossbach* and *Weber* concerning the time during which quinine remains in the blood and its concentration in that fluid, have shown that of the preparations examined Cardiazol-Quinine gives the highest concentration and is found in the blood longer than any of the other products examined. Assuming a fixed relation of concentration and time of presence in the blood to pharmacodynamic action, Cardiazol-Quinine is the preparation to be preferred.

TRADE PACKINGS

Cardiazol tablets	Tubes of 10
	Hospital packings of 100
Cardiazol liquid	Bottles of 10 gm.
	Hospital packings of 100 gm.
Cardiazol ampoules ...	Boxes of 3
(1·1 c.c.)	Boxes of 6
	Hospital packings of 30
	Hospital packings of 80
Cardiazol ampoules ...	Boxes of 2
(3 c.c.)	Hospital packings of 10
	Hospital packings of 30
Cardiazol ampoules ...	Boxes of 2
(5 c.c.)	Hospital packings of 10
	Hospital packings of 30
Cardiazol powder.....	Bottles of 1/4 oz.

Hospital packings are supplied at substantially reduced prices.

Cardiazol-Quinine in bronchitis and bronchopneumonia (oral doses in the slighter forms) as well as in other catarrhal disorders, e.g., angina and influenza. *Agostoni* describes the favourable influence of Cardiazol-Quinine in 15 cases of respiratory disorders (pneumonia, bronchopneumonia, influenza). The success was particularly marked in subacute cases. 2–4 dragées daily effected a marked improvement in the general condition. The temperature fell slightly, the respiratory function was improved, the pulse gained in force, blood-pressure and diaphoresis were favourably influenced. In serious cases (lobar pneumonia, septic bronchopneumonia) with marked cardiac insufficiency, cardiotonics of greater potency had to be given simultaneously. *Mattirolo* reports good results from Cardiazol-Quinine in lung disorders (croupous pneumonia, bronchopneumonia, influenza, etc.). He gave 2–3 injections in the space of 24 hours; they reduced the temperature, improved the respiratory and cardiac activity and the general condition. *Pugnani* relates his success with Cardiazol-Quinine in acute and chronic bronchial and bronchopulmonary affections, more particularly influenza. In lobar pneumonia the medication abolished dyspnœa, reinforced the cardiac function and reduced the pulse-frequency, enabling patients to pass through the critical stage with greater ease. In the treatment of pneumonia, *Eimer* always administers quinine in addition to serum treatment, in the form of Cardiazol-Quinine, i.e., 4 c.c. of the combination (= 1 gm. quinine), daily by intramuscular injection. *Reig Cerdá* is of opinion that Cardiazol-Quinine renders valuable services in the treatment of pneumonias and bronchopneumonias, more especially where the general condition of the patients is seriously undermined. The antithermic effect of the preparation is sure and persistent, the tonicizing

CLINICAL EXPERIENCES

INTERNAL MEDICINE

A. Infectious diseases

I. Infectious diseases of the respiratory organs

(a) Bronchitis, (broncho-)pneumonia

Birkenholz treated a number of patients suffering from pneumonia and febrile, dense bronchitis with Cardiazol-Quinine (2 dragées thrice daily, or 2 ampoules daily, injected intramuscularly or intravenously). The *general condition of the patients* thus treated improved in marked manner. Expectoration grew freer and apyrexia followed promptly. The Cardiazol-Quinine combination, injected intramuscularly or given per os, has also been much used by *Nathan*, more especially in the slighter forms of catarrhal affections of the upper respiratory passages, the frequent cases of senile bronchitis and bronchopneumonia, and in influenza and influenza-like disorders. The dosage was 2–3 Cardiazol-Quinine dragées, twice or thrice daily, or 1 ampoule, once or twice daily, according to the severity of cases. In bronchopneumonia, injections were the rule; else the otherwise usual quinine combinations were given. *Friehs* prescribes Cardiazol-Quinine in bronchitis (also infantile bronchitis), including all transitions to croupous or postoperative pneumonia. Complete apyrexia or a fall in the temperature ensued in a few days. *Schreiber* speaks of good results with

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action on the circulation conspicuous. *Kratzenberg* also prescribes Cardiazol-Quinine in pneumonia. He mentions an acute case of great severity which came for treatment in the initial stage and in which the excellent effect of the preparation was clearly demonstrated. The temperature was forced down, the attack visibly cut short and the *number of pneumococci radically reduced. Gundel* and *Seitz'* experiments have proved that Cardiazol-Quinine displays a strongly bactericidal action on highly virulent pneumococci of every type. Cardiazol-Quinine injections are advised by *Franck* in croupous pneumonia. *Thannhauser* mentions the same indication. *Heimberger* speaks of Cardiazol-Quinine as an extremely reliable and well tolerated medicament for the treatment of pneumonia. *Flaum* administers Cardiazol-Quinine dragées throughout the course of all serious forms of pneumonia and recommends the medication for many infectious diseases associated with a high temperature.

According to *Haţieganu*, Cardiazol-Quinine renders eminent services in infectious disturbances of the lesser circulation (bronchitis, pulmonary congestions). Cardiazol, combined with quinine, influences both the circulatory disturbances and the infectious state of the lungs. The mutual complementation of effects improves the circulatory function and results in a more adequate oxygen supply.

(b) Influenza

Birkenholz regards the Cardiazol-Quinine medication as an important advance in the treatment not only of pneumococcal pneumonia but also of influenzal pneumonia and febrile bronchitis. He also favours the early treatment with 3–4 Cardiazol-Quinine dragées daily of influenza without the pneumonia complication.

Crohn describes an influenza epidemic during which he gave Cardiazol-Quinine (dragées and ampoules) in a series of influenzal pneumonia cases. In the more serious forms he injected 2 c.c. twice or 1 c.c. thrice daily. The course of the illness did not appear to be shortened by the medication, but, as *Crohn* says, that could hardly be expected in view of the small quinine dosage. The intention, moreover, was to exert an antitoxic (bactericidal or growth-inhibiting) influence, apart from supporting the circulation by Cardiazol. *Schreiber* tells of about 100 cases of lobar pneumonia during an influenza epidemic which he treated with Cardiazol-Quinine injections. In contrast with other quinine preparations he observed no local irritant symptoms. He mentions his impression that Cardiazol-Quinine shortened the illness, also that the crisis was less brusque and less marked by attacks of perspiration and acute cardiac debility than usually seen. Where the remedy was administered early enough it succeeded in aborting the disorder. *Nathan* also describes the use of Cardiazol-Quinine during an influenza epidemic. He gave it to most of his influenza patients and to the numerous angina cases seen at the time. In the milder forms, Cardiazol-Quinine was given per os; in bronchopneumonia by intramuscular injection. The invariably favourable effects of the Cardiazol-Quinine medication were seen in the disappearance of the subjective discomforts, the relatively early fall in the temperature, the conspicuous improvement in the circulation (especially after injections), the greater ease of expectoration and the repression of the florid inflammatory symptoms. *Hegler* considers the Cardiazol-Quinine dragées extremely useful in influenza also from the practical point of view. *Friehs*, who had successfully tried the Cardiazol-Quinine dragées against influenza on himself,

both prophylactically and therapeutically, gave the remedy in numerous *influenza cases* with *corresponding success* (he had taken up to 10 dragées daily without experiencing secondary effects). *Gavrilă* treated numerous cases of (uncomplicated) influenza with 1–3 Cardiazol-Quinine dragées, twice to thrice daily, or, where patients developed high temperatures, with 1 to 2 intramuscular injections daily. The temperature fell fairly promptly and pulmonary complications were prevented. In influenza cases with lung complications, 2–3 Cardiazol-Quinine injections daily were necessary.

Stanca and *Gherman* state that Cardiazol-Quinine, given in good time and in sufficient dosage (2 c.c. immediately, by intramuscular injection) is able to combat influenzal or catarrhal infections with rapidity. The preparation also helps to prevent complications and to remove the latter where already existent. *Muhlens* prevents pneumonia in influenza by injecting 0·5 gm. quinine (in cardiac debility, Cardiazol-Quinine by preference) intramuscularly into the posterior upper quadrant of the musculature of the nates. This is done immediately on admission of a patient and the injection repeated on the same day and on following days if required. *Muhlens* speaks of 10 cases subjected to this treatment (some with a temperature of 40–41° C.), in which a *single* injection sufficed to abort the infection and to prevent complications.

Ulrich administered Cardiazol-Quinine in 4 cases of "double" influenza. No complications ensued, the cases ran a benign course and, above all, there was not the slightest suspicion of even the smallest pneumococcal focus.

(c) Pulmonary tuberculosis

Grünewald speaks of satisfactory results from Cardiazol-Quinine (dragées) treatment of pulmonary tuberculosis. The temperature is gently reduced by the simultaneous central and peripheral influence of the preparation, the process being unaccompanied by sweating attacks. Equally noteworthy is the generally stimulant action of quinine. The administration of quinine together with a circulatory tonic is useful because the heart requires roboration, especially in febrile tuberculosis running a chronic course. Cardiazol-Quinine dragées are also recommended by *Schröder* in the treatment of pulmonary tuberculosis associated with circulatory disturbances. *Pugnani* used the preparation in a number of cases of tuberculo-toxic tachycardia.

Geiger investigated the prophylactic value of Cardiazol-Quinine against post-operative complications (especially pneumonia) after *thoracoplastic operations.* The contrast between the Cardiazol-Quinine-treated and the untreated cases was marked: although the former were, on the whole, cases of a serious nature, they nevertheless ran a much more favourable course (much higher percentage of cases without complications and incomparably lower percentage of incidence of the much-dreaded post-operative pneumonia).

II. Other infectious diseases

(a) Otorhinolaryngological infections

Bey-Id has made particular use of Cardiazol-Quinine (dragées or ampoules) in infectious diseases. In acute, febrile affections such as *tonsillitis, angina, bronchitis, tracheitis, rhinitis acuta, influenza* and other infectious disorders, he observed that the medica-

both prophylactically and therapeutically, gave the remedy in numerous influenza cases with corresponding success (he had taken up to 10 dragées daily without experiencing secondary effects). *Gavrilă* treated numerous cases of (uncomplicated) influenza with 1–3 Cardiazol-Quinine dragées, twice to thrice daily, or, where patients developed high temperatures, with 1 to 2 intramuscular injections daily. The temperature fell fairly promptly and pulmonary complications were prevented. In influenza cases with lung complications, 2–3 Cardiazol-Quinine injections daily were necessary.

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20 typhoid cases treated with Cardiazol-Quinine, mostly per os, 3–5 dragées daily, occasionally also per injectionem. This medication was successful in keeping the temperature within moderate bounds. The general condition remained good and there were no complications. In serious cases he gave 2–3 injections; also further cardiotonics where required. *Fahrenkamp* speaks of Cardiazol-Quinine as a simple and reliable antipyretic in typhoid. The therapy is also recommended by *Băltăceanu* in typhoid associated with myocarditis.

(c) Malaria

Tropp is in the habit of giving an intramuscular quinine injection, often in the form of Cardiazol-Quinine, in malaria cases (especially in tropica) with alarming symptoms immediately patients are admitted. *Hegler* and *Nauck* recommend injections of quinine, including Cardiazol-Quinine, in all malaria cases with gastro-intestinal absorptive deficiency, e.g., in violent vomiting, diarrhœas or dysenteric complications. *O. Fischer* writes that the combination of quinine with Cardiazol is of excellent service in malaria. Seeing that intravenous injections of quinine, the only remaining useful measure in grave cerebral malaria with unconsciousness (coma), frequently damage heart and circulation, *O. Fischer*[1] advocates the simultaneous administration of a circulatory tonic and mentions Cardiazol-Quinine as particularly suitable. The quinine is, in these cases, injected slowly and in high dilution. *O. Fischer*[2] favours Cardiazol-Quinine very particularly also in quinine prophylaxis. According to *Agostoni*, the preparation is most serviceable to combat circulatory insufficiency in sufferers from various forms of malaria, including inoculated malaria.

tion not only lessens the infection rapidly but frequently aborts it. Anginas and tonsillitis cases in the early stage and exhibiting a tendency to abscess formation are often cured by the Cardiazol-Quinine medication. In the milder forms the dosage given was 1 Cardiazol-Quinine dragée thrice daily until apyrexia was reached. In angina and tonsillitis with a tendency to abscess formation, as well as severe forms of laryngitis, bronchitis, commencing *serous inflammation of the middle ear*, influenza, pyrexia after operations, and in various other serious disorders, he gave 2 Cardiazol-Quinine dragées thrice daily, in grave cases also up to 2 dragées every 2 hours. Patients who had difficulty in swallowing received 1—3 Cardiazol-Quinine injections, intramuscularly, every day, according to requirements. *Gavrilă* had good results from the Cardiazol-Quinine medication in uncomplicated catarrhal or follicular tonsillitis (10 cases). He gave 1—2 intramuscular injections daily. *Friehs* describes the favourable action of Cardiazol-Quinine in 3 cases of *otogenic sepsis* and in one case of *sinus phlebitis*. Intramuscular and simultaneous oral Cardiazol-Quinine treatment visibly improved a case of *septicopyæmia following angina.*

(b) Typhoid fever

Geller gives his typhoid patients 1 Cardiazol-Quinine dragée 3—6 times daily (4 dragées suffice in the majority of cases). This medication keeps the temperature within moderate limits and somnolent or deliriant states do not develop. Occasionally there is some slight drowsiness and apathy. The fall in the temperature caused by Cardiazol-Quinine saves energy and facilitates the care of patients, especially in respect of alimentation, the latter favoured by their awareness and the state of rest. *Gavrilă* describes

writer continues the Cardiazol-Quinine medication as a supporting measure for two months, giving 3 dragées daily during alternate weeks, interposing digitalis if indicated. *Agostoni* says that in certain cases of disturbed rhythm intracardial conductivity is favourably influenced by Cardiazol-Quinine. *Pugnani* reports that a course of Cardiazol-Quinine, varying from 10 to 30 days, restores normal rhythm completely in cardiac arrhythmia and that the remedy raises the vascular tonus at the same time. In cases of slight decompensation, the mere regularization of the cardiac function and stimulation of diuresis effected by Cardiazol-Quinine sufficed to cause the disappearance of œdema, cyanosis and dyspnœa. Cardiazol-Quinine in doses of 3 dragées daily for 2—4 or, at most, 6 days is recommended by *Mayr* against arrhythmic disturbances. In serious arrhythmias with decompensation, he gives two doses of 0·1 gm. quinidine on the day preceding the Cardiazol-Quinine medication because this improves the quality of the subsequent quinine action. In the further course he uses digitalis. In complete arrhythmia, larger doses are necessary (4—8 dragées daily for a week), after which digitalis is given. After improvement of the arrhythmic state the heart must be controlled for several months during which Cardiazol-Quinine is often usefully given from time to time for periods of 2—3 days. The Cardiazol-Quinine combination has been successfully given by *Segrè* in myocardial disorders associated with arrhythmia.

(b) Tachycardia

In paroxysmal tachycardia, *Heymans* uses and recommends Cardiazol-Quinine for prophylactic purposes. The intramuscular injection of *Cardiazol-Quinine* procured a prompt effect in two of

(d) Dysentery

According to *O. Fischer*[3], quinine plus Cardiazol renders valuable services also in dysentery.

(e) Psittacosis

For the treatment of psittacosis (in analogy with serious cases of pneumonia or influenza), *Hegler* advocates the early administration of quinine, best in the form of Cardiazol-Quinine, twice to thrice daily.

(f) Varicella

Gavrilă reports satisfactory results from Cardiazol-Quinine injections in 5 cases of grave varicella.

(g) Septic infections

Lurz and *Klingen* have had very good results with Cardiazol-Quinine in the treatment of disorders of a septic nature (septic abortion, ligneous phlegmon, prostatic abscesses, orchitis and febrile cystitis).

B. *Cardiovascular disturbances*

I. Cardiac arrhythmias

(a) Arrhythmia

In complete arrhythmia, *Mattirolo* gives Cardiazol-Quinine, preferably in the form of dragées, 4–8 dragées daily, for a week. If this medication brings no improvement he interposes a course of digitalis, using Digipuratum (Knoll). He then resumes the Cardiazol-Quinine treatment. A regularizing effect can only be obtained with relatively large doses. When the condition is improved, the

II. Heart disorders, circulatory debility

Agostoni reports that in certain cases of acute circulatory insufficiency due to decompensated valvular defects or serious myodegeneration, Cardiazol-Quinine was not at first able to abolish the circulatory congestion; subsequently, however, its influence proved very favourable inasmuch as it maintained the state of compensation attained. He also describes four cases of bronchial asthma and chronic bronchitis with distinct insufficiency of the right ventricle, in which Cardiazol-Quinine was of much assistance in abolishing the præcordial and epigastric pressure. In cardiorenal cases the simultaneous administration of medicaments of the purin group was found useful. 2–3 Cardiazol-Quinine dragées pro die (apart from salicylates) effected lasting improvement of the circulatory equilibrium in three cases of evolutionary rheumatic endocarditis in the subacute stage.

According to *Pugnani*, Cardiazol-Quinine renders excellent services in *hypotension* and *asthenia* associated with organic degeneration. The medication improves the cardiac function, raises vascular tonus and blood-pressure and retards the basal metabolism.

Rosner and *Kornblueh* tried Cardiazol and Cardiazol-Quinine (1–2 dragées) in *states of exhaustion following athletic exertions.* They observed that patients recovered quickly after a dose of Cardiazol, especially if given in combination with quinine. Pulse and respiration became normal and the subjective discomforts disappeared visibly.

Haeckel's patients suffering from paroxysmal tachycardia. The injection produced an abrupt alteration in the pathological aspect: the pulse frequency declined rapidly and dyspnœa improved. Paroxysmal tachycardia is also mentioned by *Löhr* as a special field of indication for Cardiazol-Quinine. *Fahrenkamp* uses Cardiazol-Quinine together with Digipuratum (Knoll) to combat arrhythmia. This medication has a favourable influence on the conductivity system and, at the same time, improves the cardiac force and the circulation.

(c) Extra-systoles

Heymans, writing on the subject of extra-systoles, especially in arrhythmia perpetua, says that Cardiazol-Quinine is frequently of great value. *Mattirolo* gives the preparation in extra-systolic arrhythmia in a dosage of 3 dragées daily for 10 days, repeating that course of treatment 3–4 times according to requirements, with pauses of a week. He reports that in a number of cases the medication, whilst not suppressing the extra-systoles altogether, yet succeeded in diminishing their frequency. *Mattirolo* further describes his treatment of extra-systolic arrhythmia with a combined Cardiazol-Quinine and digitalis medication: 3 Cardiazol-Quinine dragées daily in alternation with 2 Digipuratum (Knoll) tablets daily during 6 days. This treatment at times abolished the extra-systoles altogether. *Jagić* and *Zimmermann* state, in a publication on *strophanthin therapy*, that in many cases 3 Cardiazol-Quinine dragées pro die quickly counteract the inclination to extra-systoles though the original strophanthin dose is retained.

Quinine abolished it again by the autumn. The cause of the improvement in the blood-picture is no doubt to be sought in the addition of the tonicising effect of Cardiazol to the action of quinine.

GYNÆCOLOGY AND OBSTETRICS

Induction of labour, in the dilatation period

Kratzenberg publishes his experiences with Cardiazol-Quinine in obstetric practice. At the onset of labour in the first stage he gives 1 dragée and another dragée after 15 minutes. The dose is repeated at intervals of 1 hour. In all his cases powerful normal labour was the result. The medication was continued until rupture of the fœtal membranes resulted. It proved unnecessary to use further ecbolics, always required where pure quinine is given. Increased sensibility and better perfusion of the uterine tract are mentioned in explanation. *Kahnt* has published his experience with Cardiazol-Quinine (ampoules) in 80 obstetric cases. He found the dose of quinine contained in the Cardiazol-Quinine ampou'es to be the most efficacious. A tentative increase of the dose to 0 5 gm. quinine had less satisfactory results. The peak of the action is reached in about 30 minutes; therefore, the injections–generally 3–were given at intervals of 20–40 minutes, according to the situation. Where Cardiazol-Quinine was used, the injections never produced injurious effects on the fœtus referable to the quinine administered. The Cardiazol-Quinine injection was used only at full term and during the first stage of labour. *Kleff*'s method of inducing labour is to give 1 Cardiazol-Quinine ampoule, twice or thrice at $^1/_2$-hourly intervals, and to combine this medi-

Mattirolo describes the effects of Cardiazol-Quinine in *tachycardia in patients suffering from Graves' disease.* He gave it in alternation with Lugol's solution (2–3–5 cgm. iodine pro die, for 2 weeks, 3–4 Cardiazol-Quinine dragées, daily, during the third week). This treatment maintained the improvement achieved by the administration of iodine also during the week in which patients received no iodine. A case of hyperthyroidism is cited by *Agostoni.* The prolonged use of Cardiazol-Quinine resulted in a certain slowing of the pulse and the abolition of a systolic apex bruit which had been present for more than a month. *Pugnani* has also prescribed Cardiazol-Quinine with success in some cases of Graves' disease for the purpose of reducing the pulse frequency. According to *Mayr*'s experience, Cardiazol, and especially Cardiazol-Quinine, are of much assistance in regulating the cardiac function in Basedow patients who tolerate digitalis badly.

Addendum: *Anæmia.*

From observations upon herself, *Lüttger* reports that, in hyperchromatic anæmia, a dose of 2 Cardiazol-Quinine dragées daily (remedy highly esteemed and regularly prescribed by her as a reliable influenza prophylactic) produced a marked rise in the hæmoglobin content (Sahli) and the erythrocytes count after only 14 days and that the blood-picture continued to improve. She took no other medicament apart from Cardiazol-Quinine. The disorder returned in the following spring after the medication had been discontinued, but regular doses of Cardiazol-

diazol-Quinine injections are given because of their rapid and powerful effect. *Nordmeyer* gives 1 Cardiazol-Quinine dragée 4 times, at intervals of 1 hour, during the first stage, so as to increase the response of the uterus to labour stimuli and ecbolics during "twilight sleep".

Meder recommends Cardiazol-Quinine to promote labour also in *overdue cases.*

Primary uterine inertia, premature rupture of bag of waters

In primary uterine inertia and premature rupture of the fœtal membranes, *Lang* gives his patients 1 Cardiazol-Quinine dragée, followed by another after 1 hour. In only very few, partly obstinate, cases has he found it necessary to administer 2 more dragées at hourly intervals *P. Weiss* relates his experience with Cardiazol-Quinine in a large number of obstetric cases. His observations mainly concern primary uterine inertia and premature rupture of the fœtal membranes. In feeble labour during the first stage the action of the preparation is considerably better and less liable to cause damage than hypophysis (posterior lobe) preparations. In these cases 2 Cardiazol-Quinine dragées, the second 1 hour after the first, were administered. It was only rarely necessary to supplement this medication by a further 1—2 dragées at hourly intervals. More than 4 dragées have never been required to obtain the desired effect. In the treatment of primary feeble labour and to induce labour, as well as in cases of premature rupture of the fœtal membranes, abortus and premature birth, *Boesze* gives Cardiazol-Quinine, preferably in the form of suppositories (1 suppository, 3 times daily) or else by intramuscular injection. In all cases (of middle-aged primiparas) with premature rupture of mem-

cation with various other therapeutic measures. First of all he places his patient in a hot bath and gives her castor oil. After 1 hour he commences the intramuscular application of Cardiazol-Quinine, giving 3 injections at $^1/_2$-hourly intervals; then, two hypophysis preparations ($^3/_4$–2 Vögtlin units) alternately, at intervals of 30–60 minutes, several times if required. It may be necessary at times to balloon the cervix between the second and third hypophysis doses. Cardiazol-Quinine has also proved very valuable in feeble labour during the first stage. The preparation is especially indicated for parturient women with general constitutional debility in view of the clearly observable tonicising action of the Cardiazol. As far as influenza-infected parturient women are concerned it is not too much to look upon Cardiazol-Quinine as the remedy of choice. 1 ampoule is injected every 30–60 minutes, up to 5 times. In circulatory and other disturbances in the mother or infant (purely mechanical disorders excepted) Cardiazol-Quinine is not only an efficient ecbolic but also the best agent to promote improvement of the fœtal heart sounds. Also *Hansen* speaks of the beneficial influence of Cardiazol-Quinine in the first stage and for the induction of labour (4 to 6 doses). *Tubio de la Torre* gave Cardiazol-Quinine dragées where pains failed to set in, and, more particularly, when the temperature rose at the same time; also in cases of premature birth. *Tollas* also gives Cardiazol-Quinine dragées to induce labour and during the first stage. *Vidaković* advocates the use of Cardiazol-Quinine in obstetrics for the reason that quinine increases uterine sensibility and exerts an antipyretic action in sub-febrile partus whereas Cardiazol diminishes the danger of intra-uterine asphyxia. In the second stage, intramuscular Car-

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branes and complete absence of pains, he found that the introduction of a single suppository was followed, after 20 minutes, by the onset of most satisfactory pains so that the partus was completed in the course of 2–3 hours. In primary uterine inertia a Cardiazol-Quinine suppository was often the sole medication required. In some cases 2–3 suppositories had to be given during 24 hours, occasionally even in combination with injections of a hypophysis preparation, so as to obtain the desired effect. *Meder* recommends the administration of 1 Cardiazol-Quinine dragée hourly in primary feebleness of labour. A pause of several hours is advocated after the fourth or fifth dose. In view of the heightened sensibility of the uterus caused by the quinine the adjuvant use of ecbolic hormones can be kept in very small compass. Success is generally very prompt. In secondary uterine inertia, the use of larger quinine doses (2 Cardiazol-Quinine dragées, up to 3 times if necessary) is advised. In these cases the dosage of the other ecbolics (hypophysis preparations) may also be raised seeing that the aim is a speedy termination of the partus. The nature of each single case must, of course, determine the appropriate dosage. *Tůma* gave Cardiazol-Quinine to induce labour and uterine contractions after premature breaking of the waters, either in doses of 1 dragée every $^1/_2$-hour, up to 4 dragées, or 2 dragées, three times, also at $^1/_2$-hourly intervals. In other cases injections of hypophysis preparations were necessary. *Hüssy* recommends combating primary uterine inertia with quinine in order to render the uterine musculature more susceptible to the influence of pituitary preparations. Among quinine products he favours Cardiazol-Quinine. Since he has used this he has never observed any untoward effect on the fœtal heart sounds. *Gamstätter* has also administered

Cardiazol-Quinine dragées in primary inertia and premature rupture of the fœtal membranes. He observed that the Cardiazol-Quinine combination accelerates the onset of action by 10 to 15 minutes and intensifies labour. Apart from this, the preparation is extremely well tolerated. His rule is to give 3 dragées at intervals of 1 hour. Vomiting was experienced only very rarely and only by very sensitive and agitated women. *Holtermann* also uses Cardiazol-Quinine (2 dragées or 1 ampoule, three times, at intervals of one hour) for the induction of labour in premature rupture of the bag of waters.

Abortion, premature delivery

P. *Weiss* describes the use of Cardiazol-Quinine in gynæcology to induce abortion and premature birth, as well as in the treatment of complications. During the first 3 months of pregnancy, 4 Cardiazol-Quinine dragées, given at intervals of 1—4 hours, generally produce the desired result after at most 24 hours. Where necessary the medication can be followed by the administration of pituitary (posterior lobe) preparations. Every case of febrile abortion was at first given a course of Cardiazol-Quinine, generally accompanied by conservative treatment. If this did not result in apyrexia, operative measures were resorted to. In a few cases of partial placenta retention running a febrile course, the Cardiazol-Quinine medication was not always able to bring complete success but it was at any rate able to reduce the temperature to normal in a relatively short time and to loosen the fœtal membranes so that they were easily removed by operation. Cardiazol-Quinine has been tried also by *Lang* in a series of abortion cases. He says that the remedy has rendered him good services in the

sense of conservative therapy, more especially in the treatment of febrile abortion. Accordingly, a trial with Cardiazol-Quinine dragées is recommended in every case of febrile abortion before operation is undertaken. In nearly all cases the abortion could be carried through with the same doses as used for a normal partus. Curettage was always able to be delayed until the temperature had fallen to normal. *Lang* stresses the point that Cardiazol not only greatly increases quinine tolerance but that the Cardiazol component is of especial advantage in regard to the fœtal heart sounds and, in febrile abortion, to the maternal circulation. *Gamstätter* has likewise used Cardiazol-Quinine with excellent results in the treatment of abortions. He never fails to give it in febrile abortion and is almost always able to effect expulsion in a conservative manner or at least to ensure apyrexia within a few days. Even where patients had received 3–4 dragées daily for several days, there were no complaints of secondary quinine effects such as nausea, vertigo and tinnitus. *Frommolt* mentions that in Stoeckel's Clinic in Berlin every abortus with an axillary temperature of more than 38° C. at the commencement of the treatment, is excluded from active treatment and that spontaneous expulsion is promoted by doses of quinine, etc. (Cardiazol-Quinine, given orally or by injection). *Kleff* always uses Cardiazol-Quinine in febrile abortion where spontaneous expulsion of the uterine contents within the limits of conservative therapy is to be expedited. The dosage is 1 ampoule every $^1/_2$–1 hour until the desired effect is obtained. *Meder* has almost invariably seen excellent results from 2 Cardiazol-Quinine dragées, given thrice daily, in febrile abortion or pyrexia after spontaneous or artificial abortion: The last shreds of fœtal membrane were expelled *after 1–2 days and the tem-*

perature declined. In highly febrile, incomplete, abortion, Cardiazol-Quinine is, in *Meder's* view, the medication of choice. Active measures can only be recommended in the presence of very severe hæmorrhage. The application of a firm vaginal tampon and the use of Cardiazol-Quinine will be found particularly useful where the os uteri is constricted. *Galve Raso* also recommends Cardiazol-Quinine in the treatment of abortion. His method (a modification of Schröder's method) consists in the administration of 2 Cardiazol-Quinine dragées, 4 times at intervals of 1 hour, after which he gives 3–5 units of pituitrin injected twice with an interval of 1 hour. This procedure enables him to reduce the number of abortions calling for surgical treatment to a minimum.

Childbed-fever, Lochiometra

In *childbed-fever Boesze* observed improvement in the general condition and appetite after the administration of Cardiazol-Quinine. The temperature fell by 0·5–1·5° C. The pulse became stronger and of better quality and convalescence was speedy. In one case of puerperal sepsis the patient's condition was rendered relatively tolerable for 3 weeks by the administration of Cardiazol-Quinine. *Fragoso* has used the remedy, in a dosage of 3 dragées per diem, with good success in 14 cases of puerperal endometritis. *Kahr* also reports excellent results from Cardiazol-Quinine (dragées) in endometritis.

Meder praises the effects of Cardiazol-Quinine in *lochiometra*. He advocates supporting the medication by reduced doses of some ergot preparation.

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shock favour their appearance. Improvement in the general condition and that of the lungs was observed during the first 24 hours following a Cardiazol-Quinine injection. The subjective discomforts disappeared. The temperature fell after one to three days, expectoration was facilitated and the florid inflammatory symptoms receded. Cardiazol-Quinine rendered good services also where examination of the lung revealed beginning hypostatic pneumonia. The treatment of serious cases was always complemented by injections of Cardiazol or the administration of hypertonic glucose and physiological salt solutions. *Henschen*, *Bucher*, *Christ* and *Szanto* have also had good results with Cardiazol-Quinine in post-operative bronchitis and pneumonia. The favourable action of Cardiazol-Quinine (ampoules and dragées) in post-operative pneumonia is mentioned also by *Americo Valerio*. *Schranz* writes that post-operative bronchitis has not been seen since pre-operative, intramuscular, injection of 1 c.c. Cardiazol-Quinine was made the invariable rule for all operation cases. Patients afflicted with a slight catarrh on admission are given intramuscular injections of 1–3 c.c. (according to severity) also on succeeding days. The effect on elderly patients is described as particularly notable inasmuch as the Cardiazol-Quinine exerts a certain tonicizing action whilst, at the same time, it prevents circulatory complications. When he wrote his article, *Schranz* had experience of 1500 Cardiazol-Quinine-treated cases. *Simon* found that post-operative lung complications cannot be entirely prevented by Cardiazol-Quinine but he gained the impression that the course of prophylactically premedicated bronchopneumonia and pneumonia is milder and of shorter duration. In established bronchopneumonias and pneumonias Cardiazol-Quinine is given

Treatment and prophylaxis of post-operative complications

(a) Bronchitis, pneumonia

Peters has tried Cardiazol-Quinine (dragées and ampoules) in post-operative bronchitis and pneumonia. His impression is that the remedy exerts a decidedly favourable influence on these conditions and, to all appearances, is also of considerable prophylactic value. *Friehs* says that the action of Cardiazol-Quinine is particularly striking in recent post-operative pneumonia, especially where both lungs are affected. Since he has used the remedy he has not lost a single patient through this complication. It appears essential to give it in liberal dosage (1 ampoule morning and evening, and 2 dragées, thrice daily) and from the earliest possible moment. *Paulino* first gave Cardiazol-Quinine post-operatively in cases of established lung complications but subsequently resorted to its use as soon as there was a rise in the temperature. Where Cardiazol-Quinine was given in good time (1 or 2 ampoules daily) the pulmonary complications ran a distinctly milder course. On the strength of the favourable results obtained Cardiazol-Quinine is recommended as a reliable medicament with which to combat or prevent post-operative complications. *Vohnout* gives Cardiazol-Quinine (1—2 intramuscular injections daily) for the prevention of post-operative lung complications and does not confine the medication to cases where a rise in the temperature and objective findings indicate the development of such complications, but administers the remedy also where a patient's constitution or surgical

shock favour their appearance. Improvement in the general condition and that of the lungs was observed during the first 24 hours following a Cardiazol-Quinine injection. The subjective discomforts disappeared. The temperature fell after one to three days, expectoration was facilitated and the florid inflammatory symptoms receded. Cardiazol-Quinine rendered good services also where examination of the lung revealed beginning hypostatic pneumonia. The treatment of serious cases was always complemented by injections of Cardiazol or the administration of hypertonic glucose and physiological salt solutions. *Henschen*, *Bucher*, *Christ* and *Szanto* have also had good results with Cardiazol-Quinine in post-operative bronchitis and pneumonia. The favourable action of Cardiazol-Quinine (ampoules and dragées) in post-operative pneumonia is mentioned also by *Americo Valerio*. *Schranz* writes that post-operative bronchitis has not been seen since pre-operative, intramuscular, injection of 1 c.c. Cardiazol-Quinine was made the invariable rule for all operation cases. Patients afflicted with a slight catarrh on admission are given intramuscular injections of 1—3 c.c. (according to severity) also on succeeding days. The effect on elderly patients is described as particularly notable inasmuch as the Cardiazol-Quinine exerts a certain tonicizing action whilst, at the same time, it prevents circulatory complications. When he wrote his article, *Schranz* had experience of 1500 Cardiazol-Quinine-treated cases. *Simon* found that post-operative lung complications cannot be entirely prevented by Cardiazol-Quinine but he gained the impression that the course of prophylactically premedicated bronchopneumonia and pneumonia is milder and of shorter duration. In established bronchopneumonias and pneumonias Cardiazol-Quinine is given

in the first place. *Dittmar* speaks of his favourable experience with Cardiazol-Quinine in the prevention of post-operative complications. He gives it both prophylactically and *immediately* after operation in every case of sciatic scoliosis redressment performed under an anæsthetic, and continues the medication for some days after (injections during the first week, 2 dragées, thrice daily, afterwards). He describes 25 cases treated in this manner with complete absence of complications, one case only excepted.

(b) Thrombosis, embolism

Lurz and *Klingen* invariably administer Cardiazol-Quinine for the prevention of post-operative complications. The medication not only has a favourable influence on the curative process and prevents complications on the part of the respiratory tract in practically every case, but affords the striking observation that thrombosis and embolism, formerly of relatively frequent occurrence, never appear where Cardiazol-Quinine has been given. Cardiazol counteracts a slowing of the blood-stream; quinine prevents the infections which play so important a part in the formation of thrombi. Another factor is the thrombolytic action of quinine. *Mutschler* points out that the favourable influence of Cardiazol-Quinine as a prophylactic of thrombosis has been emphasized by various authors in recent times. This agrees with his own experience of only two thrombosis cases in his orthopædic clinic during the last 15 months and in these 2 cases prophylactic Cardiazol-Quinine treatment had been neglected. The ability of Cardiazol-Quinine to diminish the liability to thrombosis is also confirmed by *Friehs*.

PEDIATRICS

(a) Bronchopneumonia, pneumonia

Bassiakos has prescribed Cardiazol-Quinine in numerous cases of infantile bronchopneumonia and is much gratified by the results. The first injection was invariably followed by a fall in temperature and rapid regression of the general and local symptoms. *Rubio* and *Palomares* describe the effects of Cardiazol-Quinine (ampoules) in 23 cases of infantile bronchopneumonia, the patients' ages being between 6 months and 3 years. The single dose injected was $^1/_2$ c.c. throughout. The administration was immediately followed by a decline in the temperature; the excessive respiratory rate decreased and the general condition improved. If necessary, another $^1/_2$ c.c. of Cardiazol-Quinine was injected on the second day of treatment, and on still further days where the condition demanded it, until the temperature ceased to rise after the action of the quinine had passed off. Mortality was considerably lowered by this therapy. *Bambouris* also speaks of the advantages of Cardiazol-Quinine (ampoules) in the treatment of bronchopneumonia in infants. *Rheindorf* advocates (i.a.) Cardiazol-Quinine in infantile bronchopneumonia.

Bosch writes that Cardiazol-Quinine is most useful in infantile pneumonia. *Lust* gives it in infantile croupous pneumonia associated with cardiac insufficiency. *Nitti* mentions Cardiazol-Quinine among the remedies useful in infantile lobar pneumonia.

(b) Influenza

Laurinsich prescribes Cardiazol-Quinine (ampoules or dragées) in infantile influenza. *Lages Netto* administers the preparation to infants suffering from influenza with protracted hyperpyrexia.

(c) Whooping-cough

Kundratitz recommends a combination of vaccine therapy with Cardiazol-Quinine, etc., in advanced cases of whooping-cough (pathologico-anatomic alterations in the respiratory organs caused by endotoxins). *Gavrilă* has also had good results from Cardiazol-Quinine in whooping-cough (the medication combined with vaccine therapy in a number of cases). His impression is that after Cardiazol-Quinine the cough paroxysms occur at longer intervals and that bronchopneumonic complications are avoided.

(d) Scarlatina

Gavrilă describes about 100 scarlatina cases, from the gravest forms with toxic and septic manifestations down to the mildest cases, in which he gave Cardiazol-Quinine either as the sole medication or in combination with serum treatment. The dosage varied between 1 c.c. Cardiazol-Quinine, injected intramuscularly, twice to thrice daily (young children $^1/_2$ c.c.) in grave cases with pulmonary and other complications, and 1–2 dragées, twice to thrice daily, in the milder forms. The value of the therapy was especially conspicuous in the graver cases where the medication helped the patient over the critical time with greater ease.

(e) Measles

In 30 cases of measles of the slighter forms, *Gavrilă* used Cardiazol-Quinine exclusively in the dragée form, giving 1–2 dragées thrice daily. In more severe disorders associated with high temperatures, marked catarrhal symptoms, etc., he administered Cardiazol-Quinine injections of $^1/_2$–1 c.c. daily. By this

method he was able to prevent pulmonary complications, more especially where the medication was begun at the onset of the affection.

(f) Diphtheria

Gavrilă has a record of 30 diphtheria cases in which, after specific serum therapy, he administered Cardiazol-Quinine by injection (once to thrice daily). The results were satisfactory. In grave cases he regards the addition of other cardiac and circulatory stimulants as necessary.

NEUROLOGY AND PSYCHIATRY

Malarial therapy

O. L. Weiss tried Cardiazol-Quinine in 52 cases of inoculated malaria. He speaks of striking results, the Cardiazol-Quinine combination being greatly superior to ordinary quinine in respect of speed of temperature-normalization. 8–12 febrile paroxysms were allowed to occur, according to the physical condition of patients. To cut an attack short, 1 gm. quinine and 0·5 gm. Cardiazol in the form of Cardiazol-Quinine (2 dragées, 5 times daily) was given for 5 consecutive days. The effect of Cardiazol-Quinine injections also impressed him as being more prompt and intensive in respect of cutting short attacks than in the case of quinine hydrochloride. *Weiss* remarks that Cardiazol-Quinine has extensive indications in malarial therapy. Good curative results can be achieved also in existing high-grade aortic aneurysm. The prepar-

ation is especially suitable for temperature-regularization, i.e., avoidance of excessively marked temperature elevations in feeble patients without abolishing the malarial infection altogether. In malarial therapy, Cardiazol-Quinine marks a step in advance and should be correspondingly useful also in the treatment of natural malaria. *Kolkmann*'s trials with Cardiazol-Quinine in malarial therapy are confined to patients with pathological changes in circulation and heart (aortic aneurysm, endocarditis, myocarditis). *Wherever the state of a patient evinced alarming symptoms* through a too great elevation of temperature, an intravenous Cardiazol-Quinine injection was given under observation of the necessary precautions. It was found that this procedure immediately prevented a further rise in temperature. There were a few cases in which the temperature rose by a further 0·8—1° C. after the injection, but it began to fall in a gradual manner after the lapse of an hour. Subsequent rises were not influenced in their intensity. In a number of cases where the production of a temperature of 40° C. appeared to bode ill to patients owing to circulatory and cardiac debility, injections of Cardiazol-Quinine, a few hours before the fever attack, were *able to maintain the temperature* lastingly between 38·9° C. and 39·5° C. Injections and oral application were found equally serviceable to cut short inoculated malaria, and superior to the ordinary quinine hydrochloride. The abortive treatment of the attacks generally consisted in 2 intramuscular Cardiazol-Quinine injections on the first day, 4 injections on the second day and subsequently 10 Cardiazol-Quinine dragées per os daily for 4 days.

DOSAGE

Oral application

The suitable dose for adults in infectious diseases and circulatory disorders as well as for the combating of febrile states is 1–2 Cardiazol-Quinine dragées, thrice daily. In urgent cases, 2 dragées may be given every 2 hours. Malarial treatment requires twice the above doses. Children are given 1 dragée, twice to thrice daily, on an average.

In cardiac arrhythmias, such as extra-systoles, tachycardia, etc., the preparation gives good results in doses of 1 dragée, 2–3 (–4) times daily.

As an ecbolic in primary uterine inertia, to induce the beginning of labour or abortion, the most serviceable method is the administration of 1 dragée every $^1/_2$–1 hour, up to 4 dragées daily.

The dragées are swallowed whole with a little water; as far as possible, after meals.

Injections

Adults are given a deep intramuscular injection of 1 c.c. (= 1 ampoule) once to thrice daily. In serious cases, 2 c.c., once to twice daily. The single dose for children is $^1/_2$ c.c.

It is best to give deep intragluteal injections into the glutæus medius, 2 to, at most, $2^1/_2$ fingerbreadths beneath the crista iliaca, in the continued axillary middle line.

Rectal application

1 suppository, several times daily, as required.

TRADE PACKINGS

Cardiazol-Quinine

dragées................ Tubes of 20

Hospital packings of 200

(Each dragée contains 0·05 gm. Cardiazol + 0·1 gm. quinine hydrochloride)

Cardiazol-Quinine

ampoules of 1·1 c.c. .... Boxes of 5

Hospital packings of 30

(1 c.c. = 0·1 gm. Cardiazol + 0·25 gm. quinine lactate)

Cardiazol-Quinine

suppositories† .... Boxes of 5

Hospital packings of 30

(Each suppository contains 0·1 gm. Cardiazol + 0·25 gm. quinine valerianate)

Hospital packings are supplied at substantially reduced prices.

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† Not generally obtainable

CARDIAZOL-DICODID DROPS

Relieve cough and support the circulation

PROPERTIES

Cardiazol-Dicodid Drops contain 10% Cardiazol and 0·5% Dicodid hydrochloride in aqueous solution. The preparation is for oral use only.

This combination-product unites the stimulant action on circulation and respiration and the relieving action on bronchospasms exhibited by Cardiazol with the antitussive, sedative and anodyne effects of Dicodid (Knoll). The therapeutic properties of the two components thus complement one another most felicitously and the extensive and multifarious use of the preparation requires no further explanation. The Cardiazol component also compensates any too marked depressant action of the opiate [Dicodid (Knoll)] on the respiratory function and Cardiazol-Dicodid Drops are thus suitable also for administration to very young children and infants as well as to debilitated and sensitive persons.

Briefly, it may be said that, in a sense, Cardiazol-Dicodid represents a synergism of therapeutic effects and an antagonism of secondary effects.

CLINICAL EXPERIENCES

INTERNAL MEDICINE

A. Disorders of the respiratory organs

I. Bronchitis, bronchopneumonia, pneumonia, etc.

Bloch has treated a number of patients suffering from bronchitis, bronchopneumonia, congestive bronchitis, lobar pneumonia, etc., with Cardiazol-Dicodid. The "loosening" action was described as giving welcome relief by nearly every patient. The trying cough irritation was quelled. Especially in genuine pneumonias was the Cardiazol-Dicodid action very favourable. *Schwab* and *Guizetti* tried Cardiazol-Dicodid more particularly in chronic bronchitis and emphysema. Not only were the troublesome irritative cough and shortness of breath much improved in a short time but the tough mucus liquefied rapidly and patients obtained prompt relief. A series of cases of bronchopneumonia and croupous pneumonia also benefited greatly from the Cardiazol-Dicodid medication, the sedative action on the respiratory centre, tonicisation of the circulation and promotion of expectoration being particularly conspicuous. *Bacmeister* prescribes Cardiazol-Dicodid (8–15 drops, once to thrice daily) in severe irritative cough, especially in influenza. In chronic bronchitis he administers Cardiazol-Dicodid (among certain other remedies) to give his patients a good night's rest as far as possible. He also uses the preparation

in bronchiectasis to prevent unnecessary coughing and regards the remedy as indicated also in acute genuine pneumonia with very painful cough. *Eickhoff* gives Cardiazol-Dicodid Drops in senile bronchitis and pneumonia to suppress serious cough irritation.

II. Influenza

The following combination is used by *Stollnreuther* in the drug treatment of uncomplicated influenza:

℞ Acid. benzoic. .... 0·1–0·15 gm.
solve in
Spirit. rect. .... 5·0 „
adde
Cardiazol-Dicodid Drops (Knoll) . 10 0 „
10–15–20 drops, thrice daily,
(according to age and constitution).

Popoff writes that he has had good results with Cardiazol-Dicodid in serious febrile states and in influenzal complications of the respiratory passages.

III. Pulmonary tuberculosis

In *v. Hayek*'s view, Cardiazol-Dicodid Drops are indicated in pulmonary tuberculosis where serious cough irritation requires combating and a sedative action on respiration is desired. He looks upon Cardiazol-Dicodid Drops as a felicitously chosen combination, stating that expectoration is both promoted and facilitated by the remedy. *Markowicz* writes that he has, in Cardiazol-Dicodid, found a preparation of excellent service in pulmonary

tuberculosis with copious expectoration. He has never observed secondary effects or interference with expectoration; on the contrary, the latter appears to be activated. The medicament is especially recommended for the reason that its action is superior to that of the codeine salts. 10—15 drops, thrice daily, is a sufficient dose, generally also for obstinate cases. *Klare* now looks upon Cardiazol-Dicodid as a medication indispensable in phthisis therapy and refers to its beneficial action in grave forms of phthisis associated with distressful cough irritation, especially at night-time.

Richert has used Cardiazol-Dicodid for a considerable time, more particularly in the treatment of *bronchitis* in consumptives. He finds that the combination facilitates expectoration very considerably. The addition of Dicodid (Knoll) has the valuable result of greatly diminishing the cough irritation. Marked improvement followed the medication also in many cases of non-tuberculous bronchitis. Generally speaking, patients were given 10—15 drops, thrice daily. A trial with Cardiazol-Dicodid Drops is particularly worth while in very obstinate cases where other expectorants fail to be of use.

Hernández Díaz has employed Cardiazol-Dicodid mainly in advanced cases of pulmonary tuberculosis associated with *circulatory insufficiency*; also in spontaneous pneumothorax with marked pressure and mediastinal derangement, diffuse sclerotic forms with Bard's emphysema, in asthmatic crises due to diffuse, fibrous processes in the lungs, in grave and slight forms of bronchiectasis, and so forth. He mentions the antispasmodic action on the bronchia and the tonic effect of Cardiazol on the circulation, so usefully added to the sedative effect on the cough centre. *Felsenfeld*

is of opinion that the cardiovascular disturbances in tuberculosis of the lungs demand the use of remedies which adapt the tuberculous anæmic heart to the diminished respiratory surface and so effect an equalization of blood-pressure values, too high in the lesser and too low in the greater circulation. The Cardiazol-Dicodid combination proved particularly useful for that purpose. Dicodid has the important role, by desensibilization of the respiratory centre, to enable the organism to tolerate a greater carbonic acid tension in the blood and to abolish the latter by deepening and retarding respiration whereby the heart gains time to effect the necessary compensation. *Felsenfeld* describes 20 tuberculosis cases with chronic and acute circulatory disturbances in which the Cardiazol-Dicodid medication had satisfactory results throughout. In acute disturbances 3 doses of 20 drops per diem were given at first. When compensation was reached, the dose was reduced to 10 drops 3 times daily, and the medication continued with 5 drops, thrice daily, also after patients felt completely well. In chronic cases, 10 or 5 drops, 3 times daily, were given according to circumstances. In cachectic patients a smaller number of drops is advisable, say 5–10 drops, thrice daily. On the strength of his experience *Felsenfeld* has no hesitation in regarding Cardiazol-Dicodid Drops as the remedy of choice in circulatory disturbances in tuberculous patients. *Haţieganu* reports very good results from Digipuratum (Knoll) combined with Cardiazol-Dicodid in heart-lung patients with symptoms of a beginning disturbance in the lesser circulation. He recommends the use of the same combination also in cases of arrhythmia. According to *Holdheim*, Cardiazol, in certain circumstances in combination with Dicodid, displays a stimulant action on impaired circulatory activity in phthisis. He says that

in many cases the medication cannot be too urgently recommended. *Dietlen* names Cardiazol-Dicodid as one of the medicaments employed by him in tuberculous circulatory debility.

Mazileff describes his excellent experience with Cardiazol-Dicodid in the treatment of tuberculous *hæmoptysis. Basch* says that Cardiazol-Dicodid not only quiets the cough-centre but that it has an antispasmodic action on the bronchia whilst it stimulates the circulation; also that the preparation deserves the preference in cases of profuse hæmoptysis requiring the use of narcotics. *Unverricht* finds it useful to place his hæmoptysis patients in a slightly elevated position and to quiet the violent cough irritation by the administration of Cardiazol-Dicodid Drops. This combination-product renders good services because it prevents further hæmorrhage being caused by cough paroxysms. He adds that only just enough must be given to suppress the cough irritation so that expectoration is not interfered with. The aim is to allay the irritation to a useful extent.

Rehfeldt recommends the administration of Cardiazol-Dicodid also before *puncture of extensive pleural exudates* and before *artificial pneumothorax operations*, sometimes liable to produce cough irritation and states of collapse. He also gives it after *thoracoplastic operations* to improve the circulation weakened by anæsthesia and operation, and to stimulate expectoration for the purpose of preventing retention of sputum. *Richert* says that Cardiazol-Dicodid Drops are most useful in all cases of recent thoracoplastic interference and recent artificial pneumothorax; it should be given immediately after operation when the risk of retention of the bronchial secretion has to be reckoned with. The action on the circulation is an additional advantage. *Markowicz* confirms the

usefulness of Cardiazol-Dicodid Drops after artificial pneumothorax operations.

IV. Emphysema and Bronchial Asthma

Majdrakoff reported very good success with Cardiazol-Dicodid in pulmonary emphysema. After 10 drops, given thrice daily for 2–3 days, the condition of patients improved visibly. The cough was quieted, dyspnœa diminished and the circulation improved. Expectoration was also reduced in amount. Serious cases required somewhat longer treatment. In the presence of very marked cardiac debility with congestive symptoms it is necessary to give digitalis at first [e.g., Digipuratum (Knoll) in doses of 20 drops, thrice daily]. When the circulatory troubles have disappeared the further treatment is with Cardiazol-Dicodid Drops. *Pfeiler* gave Cardiazol-Dicodid in 11 cases of emphysema and in 5 cases of bronchial asthma. He describes his results as thoroughly satisfactory and, in some cases, no less than brilliant. Dyspnœa and cough diminished considerably and the sedative action was of the utmost benefit to patients. Insufficiency symptoms of the left ventricle with œdemata, cardiac dyspnœa, etc., which so seriously try and depress patients, were not observed after Cardiazol-Dicodid. The administration of digitalis was, consequently, superfluous in the majority of cases. In regard to bronchial asthma it was observed that attacks failed to occur where the remedy was given in good time. Given in an actual attack, the latter ran a considerably milder course compared with cases where no Cardiazol-Dicodid was given. *Schübel*, *Gehlen* and *Biehler* are also in favour of the Cardiazol-Dicodid medication in asthma, their recommendation being founded on experimental findings.

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V. Pulmonary infarct, pulmonary embolism, hæmorrhagic pleuritis

The effect of Cardiazol-Dicodid in *pulmonary infarct* is reported by *Bloch* to be very favourable.

v. Hagen employed the Cardiazol-Dicodid medication in a case of grave sinistral *pulmonary embolism* for the purpose of relieving the cough irritation and supporting the circulatory function at the same time.

Bălțăceanu recommends Cardiazol-Dicodid as relieving cough in *hæmorrhagic pleuritis.*

Whooping-cough (see "Pediatrics", page 203.)

B. *Cardiac and Circulatory Disorders*

According to *Jagić* and *Flaum*, Cardiazol-Dicodid belongs to the remedies useful in general therapy of *heart disorders. Levin* recommends Cardiazol-Dicodid Drops as an excellent combination for the treatment of chronic heart cases associated with affections of the respiratory organs, cough, restlessness, insomnia, etc.

Popoff describes a few cases of heart disease in which he gave Cardiazol-Dicodid with very good results (improvement of the subjectively bad state and of the cardiac function). The remedy also rendered him excellent services in *angina pectoris* as well as in one case of *Grave's disease* in which the subjective state improved satisfactorily. The distressing tachycardia lessened considerably and anxiety was successfully quieted. *Hopmann* describes the good effects of Cardiazol-Dicodid and, occasionally, a combination of Cardiazol + Dilaudid (Knoll), in *stenocardiac conditions.*

Zak favours the Cardiazol-Dicodid medication in cases of labile hypertension tending towards *cardiac asthma.*

Dabowsky has obtained very good results with Cardiazol-Dicodid in people of advanced age suffering from *emphysema and cardiac debility.*

Schwab and *Guizetti* have used Cardiazol-Dicodid in *myocardial insufficiency with congested organs.* The action on the state of the circulation was distinctly beneficial. Other cases successfully treated with Cardiazol-Dicodid included incipient decompensated *mitral insufficiency.*

Bansi is of opinion that small doses of Cardiazol-Dicodid are occasionally required after *cardiac infarct.*

Koelsch mentions Cardiazol-Dicodid amongst the remedies used by him with success against severe pain in acute *poisoning by irritant gases with pulmonary œdema.*

PEDIATRICS

A. Whooping-cough

Aman reports that Cardiazol-Dicodid Drops quickly reduce the whooping paroxysms to a tolerable minimum. Attacks of the more serious kind no longer occurred after 2 days of the treatment. *Dabowsky* has also treated large numbers of whooping-cough cases with Cardiazol-Dicodid and reports that under the influence of this medication the paroxysms decrease in number and violence already during the first 2 or 3 days. The children become more restful, sleep better and take sufficient nourishment. On an average the illness is shortened by 1–2 weeks. In some of the cases the

action of the Cardiazol-Dicodid Drops was no less than striking. In one case of 4 weeks' standing, child, 11 years of age, the cough ceased abruptly after only a few doses of Cardiazol-Dicodid. *Pfeiler* writes of excellent results achieved with Cardiazol-Dicodid in 7 cases of pertussis. The dosage varied, according to the patients' ages (1–7 years), between 5 and 10 drops, thrice daily. The medicament was systematically given as soon as the convulsive stage was reached and continued far into the stadium decrementi. Very shortly after taking Cardiazol-Dicodid the attacks of "blue" cough diminished appreciably both in intensity and frequency. It is clear, therefore, that the remedy reduces violence and frequency of the paroxysms. *v. Hilger* writes that in his experience Cardiazol-Dicodid treatment of whooping-cough invariably diminishes the violence of the attacks in the convulsive stage and thus has a valuable influence on the young patients' general condition and reserve strength; also that complications such as bronchiolitis, bronchopneumonia, always liable to set in in view of the weakened general state of the majority of children, are prevented. In *symptomatic whooping-cough treatment*, *Fanton* obtained his best results with Cardiazol-Dicodid Drops; indeed, far superior to those observed after the use of other remedies. He deals with 22 cases in which he found the preparation to meet the therapeutic intentions in the best possible manner. It reduced the violence of attacks rapidly, improved the general condition and facilitated expectoration. No complications or signs of intolerance were observed. In general, *Fanton* recommends vaccine therapy for the initial catarrhal stage and the first 2 weeks of the paroxysmal period, stating that a symptomatic remedy, preferably Cardiazol-Dicodid Drops, may be used in addition. Vaccine treatment is al-

most always useless in feeble, neuropathic individuals and after previous tracheobronchial adenopathy; also where the paroxysms have lasted more than 2 weeks. In these cases, Cardiazol-Dicodid Drops exhibit a positively specific action and can also be combined with other methods of treatment. *Mader's* comparative experiments on infants suffering from whooping-cough merit particular attention. He treated half of his cases exclusively with Cardiazol-Dicodid, the other half with routine medicaments. It was seen that the Cardiazol-Dicodid-treated cases (pneumonia complication) ran a distinctly milder course. In the majority, intensity and frequency of attacks were reduced. The favourable influence on the vomiting occurring with attacks is especially stressed. *Amadei* gave Cardiazol-Dicodid in about 30 pertussis cases (children of 4 months to 10 years of age). The treatment effected considerable improvement in the course of a few days in every case. There were no further complications and the cases ended in complete cure. He looks upon Cardiazol-Dicodid as the best remedy in pertussis. *Keilmann* has investigated the properties of Cardiazol-Dicodid in about 200 cases of whooping-cough. To infants aged 3 months he gave 5 drops, thrice daily at first, increasing the dosage up to 10 drops, thrice daily, according to existing circumstances. He has never observed undesirable secondary effects and states that the influence on the course of the illness and on the attacks was extremely favourable. The dosage in the case of young children and those of school age was correspondingly higher, rising from 5—10 drops to 20 drops, thrice daily, according to the severity of cases, always without secondary effects, the children feeling fresh and lively. Cure was accelerated. *Kokkolatos* states that Cardiazol-Dicodid, given from the first days of the

catarrhal stage, shortens and eases the course of the illness and that the occurrence of complications (bronchitis, bronchopneumonia, spasms, cerebral disturbances, conjunctival hæmorrhage, etc.) is reduced to a minimum. He also remarks on the very favourable influence on the vomiting which, apart from being a torment for the little patients, frequently interferes disastrously with their alimentation. *Kochmann* recommends Cardiazol-Dicodid Drops in the treatment of whooping-cough and points to the ease of individual posology. *Spiliopoulos* also gives Cardiazol-Dicodid Drops in whooping-cough, 2–5–10 drops, 3–4 times daily.

B. Irritative cough, bronchitis, bronchopneumonia, pneumonia and other affections of the respiratory organs

Dabowsky writes of very good results with Cardiazol-Dicodid in *cough-irritation* associated with disorders other than whooping-cough (tuberculosis, tracheitis, tracheobronchial adenopathy). The preparation has been of much service to *Fanton* in the treatment of pertussoid *cough accompanied by vomiting* and due to tracheobronchial adenopathy, also in barking cough with *laryngeal stenosis after measles.* Cardiazol-Dicodid is also prescribed by *Glanzmann* in measles to combat the distressing cough-irritation. *B. Stern* recommends its nightly administration in all irritative states of the respiratory tract, e.g., *laryngeal and pharyngeal catarrhs*, dry and serous *pleurisy*, *pseudocroup* and against the coughing "habit" after whooping-cough. In serious *empyema* he gives Cardiazol and Cardiazol-Dicodid Drops in alternation; the

simultaneous administration of Cardiazol and Dicodid prior to *pleural punctures* is also described as very useful. *Wilke* regards Cardiazol-Dicodid Drops as very frequently indicated in the treatment of infants. Apart from the combating of coughs of every description, from simple pharyngeal cough to whooping-cough, from the trying cough irritation in influenzal lung affections to the gravest adenopathic cough, it is neuropathy which presents a wide field of indications for Cardiazol-Dicodid. The antispasmodic property of Cardiazol is, moreover, very beneficial in all disorders of the respiratory tract, especially in *spastic bronchitis*, of such frequent occurrence in infant age. Infants under 3 months are not at first given more than 1 drop, twice to thrice daily; those between 3 and 6 months of age, 2 drops, thrice daily. It has never been found necessary to give an infant more than 3 Cardiazol-Dicodid Drops three times a day. In *Wilke*'s opinion, the otherwise customary dose of 3–5 drops, thrice daily, is too high for infants. In his experience, 1–2 drops suffice in the majority of cases and the dose involves no kind of risk. He advocates adherence to a simple rule: as many drops pro dosi as the number of a child's years.

In a case of *capillary bronchitis* in a somewhat delicate child of 3, with a pathetic facial expression, livid complexion and justifying anxiety, *Aman* was able to effect prompt improvement by Cardiazol-Dicodid treatment. The illness appeared to assume a milder course, recovery was accelerated and there was no unfavourable influence on the heart. According to *B. Stern*, Cardiazol-Dicodid is very useful in *bronchopneumonia* and capillary bronchitis to combat restlessness and the persistent cough-irritation. Infants of three months or more were generally given 4–5 drops

of Cardiazol-Dicodid twice to thrice daily. Delicate infants at first received 2—3 drops and the dose was increased only if and as tolerance permitted. Alternation of Cardiazol-Dicodid Drops with pure Cardiazol, or confining the Cardiazol-Dicodid medication to the evenings to give the infants a restful night, has also been found a useful method. Cardiazol-Dicodid is recommended by *Kutter* for the treatment of bronchopneumonia in infants and very young children since it promptly abolishes circulatory congestion and influences the distressing cough-irritation very favourably. *Manicatide* mentions Cardiazol-Dicodid among the remedies employed by him against nocturnal restlessness and cough in infantile bronchopneumonias. *Frick* gives the preference to this medication in infantile pneumonia.

Reuss prescribes Cardiazol-Dicodid in doses of 1—3 drops, twice to thrice daily, for infants under 6 months, and 3—5 drops for children above that age, in *infantile influenza* where the circulation is endangered.

Moro has seen prompt effects from Cardiazol-Dicodid in 3 cases of spasmophilia with severe attacks of *laryngospasmus*, the patients being infants under 12 months of age.

Polykratis, reasoning that Dicodid (Knoll) has not only a selective action on the respiratory centre but a general sedative action on the central nervous system, advocates the Cardiazol-Dicodid medication also for cases requiring a higher Cardiazol dosage (pneumonia, enterocolitis, dysentery, bronchopneumonia). In this combination Dicodid (Knoll) appears able to reduce existing spastic states (spasmophilia, hyperpyrexia, meningitis, etc.) or to check a convulsive tendency.

C. Disorders of the digestive organs

Enterocolitis, dysentery

Moro describes a case of enterocolitis in which the action of Cardiazol or Cardiazol-Dicodid respectively proved prompt and lasting, both on respiration and on tenesmus and intestinal peristalsis. He adds that in dysentery the preparation has a markedly favourable influence on intestinal peristalsis and the rectal tenesmus which is so frequently a complication of infantile enteritis.

SURGERY

Doerfler uses Cardiazol-Dicodid in *post-operative medication*, especially after strumectomies. The remedy is also, and prominently, indicated in *septic processes* as they demand particular care in respect to preservation of the cardiac force.

Simon has had good results with Cardiazol-Dicodid Drops in painful *post-operative coughs* necessitating support of the circulation.

Durval Vianna gives Cardiazol-Dicodid against *restlessness in children after operations.*

GYNÆCOLOGY

Dysmenorrhœa

Liebmann describes the strikingly favourable effect of Cardiazol-Dicodid Drops on really grave dysmenorrhœa cases recalcitrant to all other treatment. In regard to dosage he frequently managed with 20 drops in the morning and 10—20 drops during

the late afternoon. He has never been obliged to exceed 20 drops thrice daily during, at most, 2–3 days. Capacity for work was not impaired by the medication nor did it produce somnolence, one case only excepted. Women, otherwise forced to stay in bed for one or more days owing to intolerable pains, were enabled to continue their work under Cardiazol-Dicodid treatment. The states of depression, not uncommon in typical cases, were greatly ameliorated and often gave way to euphoria. Menstrual discomforts are frequently absent in patients formerly treated with Cardiazol-Dicodid, i.e., where the medication has not been renewed. The preparation is notable also for its simultaneous, favourable influence on the circulatory action, respiration, the nervous state, etc. Cardiazol-Dicodid Drops are also recommended by *Heidler* and by *Hannes* (12–15 drops, thrice daily) for the treatment of dysmenorrhœa.

NEUROLOGY AND PSYCHIATRY

Neurotoxic manifestations

According to *Hanse*, Cardiazol-Dicodid is most useful in neurotoxic manifestation (tuberculosis, influenza and other infectious diseases) on account of its regularizing action on the circulation and its sedative effect.

Neuroses

Popoff was able to recognize the favourable action of Cardiazol-Dicodid in a number of neuroses cases associated with cardiac agitation. The medication restored a sense of comfort, the distressing sensations in the heart region disappearing.

Melancholia, depressive and anxiety states

Fuchs describes 15 cases of melancholia treated with Cardiazol-Dicodid and, on the strength of his experience, says that he would not now be without this preparation for the treatment of anxiety states in people of advanced age. *Faltlhauser* has had good results with Cardiazol-Dicodid in similar cases. *Bufe* recommends the administration of 15 drops Cardiazol-Dicodid, thrice daily, in the slighter forms of depression; he increases the dosage gradually to 45 drops, thrice daily. Depression, exacerbated in the mornings, is treated by *Wuth* with a single dose of Dicodid (Knoll) or Cardiazol-Dicodid, given in the morning. *Vera* regards Cardiazol-Dicodid as an excellent remedy in anxiety states: the Cardiazol component stimulates the impaired circulation; Dicodid exerts a sedative effect.

DOSAGE

The average dose for adults is 10–15–20 drops; for older children, 5–10 drops; for infants and young children, 1–5 drops. These doses can be repeated twice to thrice daily.

Since Dicodid (Knoll) is an opium derivative, no schematic rule in respect of dosage can be laid down, more especially where infants and young children are concerned. The degree of tolerance must be established in each individual case and small tentative doses should be given at first.

Where children object to the taste of the preparation it may be administered on lump sugar or in fruit-juice.

If at all avoidable Cardiazol-Dicodid Drops should not be taken on an empty stomach.

TRADE PACKINGS

Cardiazol-Dicodid Drops .. Bottles of 10 grammes
Hospital packings of 100 gms.

(10% Cardiazol + 0.5% Dicodid hydrochloride)

Hospital packings are supplied at substantially reduced prices.

CARDIAZOL-EPHEDRINE

For the treatment of bronchial asthma

Circulatory tonic with a central and peripheral action

PROPERTIES

Cardiazol-Ephedrine is a combination of Cardiazol and ephedrine hydrochloride (in the proportion of 0·1 gm. Cardiazol to 0·015 gm. *l*-ephedrine hydrochloride). The preparation is marketed in tablet form, as a solution for oral use and in ampoules.

The valuable therapeutical properties of Cardiazol as a general excitant and, especially, a circulatory tonic, respiratory stimulant and reliever of bronchospasms, are powerfully enhanced and usefully complemented by the addition of ephedrine whose principal pharmacodynamic effects lie in the same direction. The consequent enhancement of effect applies more particularly to the tonicisation of the circulation. Whereas Cardiazol directly attacks the vasomotor centre, ephedrine excites the sympathetic vascular nerve-endings. It follows that the 2 components complement each other's action on the vessels in the best imaginable manner.

The combination has another great advantage. As against Cardiazol, the action of ephedrine reaches its peak only slowly but is all the more persistent. The therapeutic effect of the combination is more rapid than that of an injection of ephedrine

alone and is more persistent than that of an exclusive Cardiazol injection.

Added to the purposeful complementation of the ephedrine effect by the centrally acting Cardiazol is another advantage, that of excellent toleration, the latter due to the cautious determination of the ephedrine dose and increase in tolerance by the Cardiazol addition.

CLINICAL EXPERIENCES

INTERNAL MEDICINE

A. Bronchial Asthma

I. Abortion of attacks

Doerr records the case of a serious asthma attack successfully treated with Cardiazol-Ephedrine. *Nemes* describes the prompt action of the preparation in bronchial asthma. He was able to cut short attacks within 8–12 minutes by the injection of 1 c.c. Increased motility and elevation of the diaphragm as a sequel to the medication were clearly observable also through the X-ray screen. *J. Stern* has tried Cardiazol-Ephedrine in a large number of slight as well as serious asthma attacks in people of various ages. In an attack he generally gives 1 c.c. and subsequently 10–20 drops or $^1/_2$–1 tablet, thrice daily. Repeated controls have shown that the blood-pressure remains constant after the injection as also after prolonged use of the oral medication. The onset of effect of the combination is not as rapid as in the case of adrenaline but, against that, the effect is of longer duration and greater persistence. Expectoration, moreover, remains facile without the aid of potassium iodide, a circumstance ascribed to the antispasmodic effect of the Cardiazol component on the bronchia. That effect convinces *Kese* of the Cardiazol-Ephedrine indication in all asthmatic states. Its action is successful also in cases where

an alteration of the right heart already exists. In *Kese*'s experience asthma attacks are cut short within 8–10 minutes. *Kohiyar* declares that Cardiazol-Ephedrine is more efficacious in bronchial asthma than adrenaline. He is in the habit of giving his patients series of 16 injections (1 injection daily in the late evening) using Asthmolysin* and Cardiazol-Ephedrine alternately. *Risché* also gives Cardiazol-Ephedrine in bronchial asthma, generally subcutaneously; in very serious cases, intravenously. Intravenous injection, 0·1–0·3 c.c., has never been followed by undesirable secondary phenomena in the very large number of cases recorded by him. In the slighter forms of bronchial asthma he gave the combination in the tablet and liquid forms, patients receiving 20 drops, twice to thrice daily, or $^1/_2$ tablet, twice to thrice daily. In a case of particularly distressing bronchial asthma, *François* had good results with 2 daily doses of Cardiazol-Ephedrine given during the crisis; against pain he administered Dilaudid (Knoll). This twofold medication, continued over 3 weeks, was responsible for a distinct improvement not only of the respiratory disturbance but also of the general condition and, above all, the subjective and objective disturbances due to the cardiac insufficiency. Where Dilaudid (Knoll) was given from the very onset of an attack the crisis was immediately arrested and the patient felt relatively comfortable.

Krone has tried local (endobronchial) Cardiazol-Ephedrine treatment in bronchial asthma, using the commercial liquid form; 5 c.c. was applied to each bronchus by means of an Ephraim atomizer after introduction of a Bruning tube. Trachea and bronchia had previously been anæsthetized with a 1% solution of quinine bimuriat. carb. with an addition of adrenaline. The effect was immediate; respiration became easier and the râles dis-

appeared. The duration of the improvement depended on the severity of cases. The treatment was repeated after 3–4 weeks where such repetition proved necessary. The majority of cases remained free from attacks after a single treatment.

II. Asthma prophylaxis (Status asthmaticus)

Kenner recommends Cardiazol-Ephedrine in the first place for the treatment of chronic asthmatic states and for prophylactic purposes, for the reason that the medicament is innocuous and always uniform in its action. *Stanganelli* also prescribes Cardiazol-Ephedrine in bronchial asthma (in status asthmaticus preferably in the tablet form). *Karrenberg* writes that in established status asthmaticus Cardiazol-Ephedrine is a valuable remedy. According to *Leffkowitz*, patients in the status asthmaticus with demonstrable alteration of the right heart react particularly well to the Cardiazol-Ephedrine medication. In these cases he gives the medicament in the liquid or tablet form for a fairly long time. In the acute attack he finds subcutaneous injections the best method. He emphatically warns against intravenous administration. *Jiménez Díaz* speaks of Cardiazol-Ephedrine as one of the remedies beneficial in bronchial asthma, more particularly in complications with vascular disturbances (hyposystolia, hypotension, etc.). *Hațieganu* gives the combination in disturbances of the lesser circulation associated with asthma attacks. *Popper* recommends Cardiazol-Ephedrine as a prophylactic of asthma attacks. Formerly he employed subcutaneous injections but now gives the remedy exclusively per os, in the tablet or liquid forms. Protracted oral administration, also after an attack, in a sense, results in an "armistice" during which the cause of the disorder can be system-

atically investigated. *J. Stern* also regards Cardiazol-Ephedrine as an efficient prophylactic. According to him, 10 drops or $^1/_2$ tablet, thrice daily, suffice for the slighter forms. In the more serious forms he gives twice these amounts. Most patients declare spontaneously that the preparation is of greater and more lasting benefit than anything previously given to them. The cause of this is probably to be found in the Cardiazol component. In cases of long standing, damage to the right heart doubtless always exists and the symptomatic action of Cardiazol cannot but have a favourable influence on that condition. The combination of ephedrine with Cardiazol, moreover, appears to eliminate the risk of a rise in the blood-pressure caused by a too frequent and too protracted administration of ephedrine. *Nemes* singles out the case of a girl of 12 years of age who suffered from remittent asthma attacks. She was given $^1/_4$–$^1/_2$ tablet, whereupon the attacks ceased promptly. *Nemes*, therefore, recommends Cardiazol-Ephedrine also as an asthma prophylactic; 10 drops, or $^1/_2$ tablet, 2 to 3 times daily. The effect of oral doses is more protracted. The remedy may also be used for continuous treatment because it has no injurious effects on the heart.

III. Asthma infantile

Manicatide and *Cajal* mention Cardiazol-Ephedrine among the remedies of proved value in infantile asthma.

IV. Senile asthma (with tuberculosis)

Nemes describes a case of senile asthma complicated by tuberculosis in which Cardiazol-Ephedrine liquid produced considerable improvement of the state of the heart and lungs.

Addendum: *Hay fever.*

In *Doerr*'s experience, hay fever is an indication for Cardiazol-Ephedrine.

B. *Circulatory disturbances*

I. In disorders of the respiratory organs

(a) Tuberculosis

Kenner describes his trials with Cardiazol-Ephedrine in incipient decompensation of the pulmonary circulation in tuberculosis. In acute cases he gave 2–4 subcutaneous injections of 1 ampoule daily, occasionally in combination with digitalis. In chronic dyspnœa, or for prophylactic purposes, he administered 1 tablet or 15 drops, twice to thrice daily. In the majority of cases the action set in after 5–15 minutes showing above all in relief of the dyspnœa and gradual diminution of the frequently very marked cyanosis. The subjective discomforts were at the same time much improved. Further signs of the beneficial action were a lessening of the tachycardia and a fuller pulse. *Mattausch* also reports good results from Cardiazol-Ephedrine in the treatment of circulatory disturbances in pulmonary tuberculosis. In 37 cases of this category of circulatory disturbances, 2–3 weeks of the treatment improved tachycardia by 20–30%, down to a normal pulse frequency. Existing hypotension and palpitations were abolished. The dosage given was 15 drops, or 1 tablet, thrice daily. After quieter conditions were established the dosage was cut down to 15 drops, or 1 tablet, twice daily. The same doses were given once a day for another 1 or 2 weeks after the discomforts had

disappeared. Much benefit has, moreover, been derived from oral Cardiazol-Ephedrine therapy as an adjuvant to general treatment of tuberculotoxic myocardial damage persisting throughout the course of long-standing, extensive, chronic pulmonary processes. The treatment was generally carried out in stages of 2–3 months with intermissions of 4–6 weeks. The prospects are less favourable in tuberculosis with circulatory disturbances of a secondary nature and due to mechanical causes, viz., in the large number of cirrhotic pulmonary processes, vicarious emphysemata, extensive pleural and pericardial indurations. Nevertheless, considerable relief resulted in cases of this kind (57). Here, oral Cardiazol-Ephedrine doses given for several months with short intermissions frequently produced notable relief of the respiratory difficulties, lessening of tachycardia and palpitations, increase in diuresis and, consequently, considerable subjective relief. In existing hypotension the pulse grew fuller; normal blood-pressure values were not raised. *Risché* gives Cardiazol-Ephedrine in circulatory disturbances of pulmonary tuberculosis and records excellent results. Tachycardia diminished whilst the subjective discomforts and dyspnœa were alleviated.

Discussing *artificial pneumothorax*, *Câmpeanu* advocates the intramuscular injection, where necessary, of adrenaline . . ., Cardiazol, Cardiazol-Ephedrine, etc., to combat gas-embolism. *Caralps Massó* prefers Cardiazol-Ephedrine to all other remedies in shock occurring during pulmonary surgery.

Nebias and *Oliveira* had a *phrenicectomy* patient with postoperative tachycardia and slight dyspnœa of 4 months' standing. These complaints were much improved by Cardiazol-Ephedrine.

(b) Bronchitis, pneumonia, influenza, etc.

Kenner found that Cardiazol-Ephedrine clearly supports the circulation and helps patients over the transient complication by preventing cardiac insufficiency in intercurrent disorders of the respiratory tract (especially in chronic tuberculosis) as well as in acute bronchitis, pneumonia, pneumothorax, pleuritis. He, therefore, looks upon Cardiazol-Ephedrine as a valuable agent with which to combat the various dyspnœic states of cardiac and pulmonary genesis and indicated especially to abolish discomforts and complications caused by disturbances in the pulmonary circulation. *J. Stern* describes a case of bilateral pneumonia in which Cardiazol-Ephedrine was particularly successful.

In *Risché*'s practice Cardiazol-Ephedrine has proved of notable value in *influenzal pneumonia* to which collapse is a frequent sequel. The state of the heart and lungs was much improved, respiration became freer and expectoration easier. In certain forms of influenza Rossi *Belgrano* regards Cardiazol-Ephedrine as indicated and prefers it to Cardiazol.

Risché reports that Cardiazol-Ephedrine produced relief of subjective discomforts also in *pulmonary tumor.*

Sánchez Freijo gave injections of Cardiazol-Ephedrine in a case of primary *pulmonary aspergillosis* with the result that the symptoms indicating pleural shock subsided within a few hours.

II. Cardiac and Circulatory Disorders

Doerr gave Cardiazol-Ephedrine to a patient with serious *cardiac decompensation*, unsuccessfully treated for many years with cardiacs of various kinds. He began with subcutaneous injections and continued the treatment per os, *20 drops, thrice daily. Not-*

disappeared. Much benefit has, moreover, been derived from oral *Cardiazol-Ephedrine therapy as an adjuvant to general treatment* of tuberculotoxic myocardial damage persisting throughout the course of long-standing, extensive, chronic pulmonary processes. The treatment was generally carried out in stages of 2–3 months with intermissions of 4–6 weeks. The prospects are less favourable in tuberculosis with circulatory disturbances of a secondary nature and due to mechanical causes, viz., in the large number of cirrhotic pulmonary processes, vicarious emphysemata, extensive pleural and pericardial indurations. Nevertheless, considerable relief resulted in cases of this kind (57). Here, oral Cardiazol-Ephedrine doses given for several months with short intermissions frequently produced notable relief of the respiratory difficulties, lessening of tachycardia and palpitations, increase in diuresis and, consequently, considerable subjective relief. In existing hypotension the pulse grew fuller; normal blood-pressure values were not raised. *Risché* gives Cardiazol-Ephedrine in circulatory disturbances of pulmonary tuberculosis and records excellent results. Tachycardia diminished whilst the subjective discomforts and dyspnœa were alleviated.

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to combat cardiac insufficiency in patients with a low systolic blood-pressure or in the collapse stage.

Risché has frequently observed a favourable action of Cardiazol-Ephedrine on *overdigitalized* hearts or hearts under the influence of digitalization. Patients with the gravest circulatory debility, very pronounced cyanosis, dyspnœa, marked agitation and absolute failure of diuresis were quieted by the administration of Cardiazol-Ephedrine. They felt better and got on well until strophanthin treatment (very useful according to the author) could be commenced. According to *Leffkowitz*, the Cardiazol-Ephedrine treatment suits in particular those cases in which a glucoside medication is not possible owing to previous digitalization or to heart-block.

Cardiazol-Ephedrine is among the preparations recommended by *Wollheim* for the treatment of *cardiovascular decompensation* (minus-decompensation). *Dubberstein* found that Cardiazol-Ephedrine injections exerted a prompt sedative effect on patients suffering from the gravest forms of *circulatory debility*, marked cyanosis and dyspnœa. Respiration deepened and became regular; patients moreover fell into a state of apathy so that recourse to powerful narcotic drugs such as morphine became unnecessary. The Cardiazol-Ephedrine action was especially striking in cases of decompensation aggravated as to the cardiac condition by their removal to hospital. An intramuscular injection strengthened heart-sounds and pulse. The increase in amplitude, however, was not so marked after Cardiazol-Ephedrine as after pure Cardiazol which latter causes the maximal pressure to rise but the minimal pressure to fall. *Leffkowitz* has given Cardiazol-Ephedrine in cases of circulatory debility of various genesis, *more particularly in in-*

able alleviation of the *discomforts and improvement in the subjective* condition followed. *Adhemar Barros* administered Cardiazol-Ephedrine by intramuscular injection in a grave case of organic *mitral lesion*, thereby saving the patient's life. According to *Dubberstein*, Cardiazol-Ephedrine in combination with digitalis renders valuable services in the treatment of organic *myocardial affections or valvular defects* with relative or absolute bradycardia also in the decompensation stage. He stresses the improved digitalis tolerance brought about by the Cardiazol-Ephedrine addition. He also tried the remedy in *heart-block* and *Stokes-Adams' disease* and observed that slow intravenous injection not only results in immediate abortion of an attack but that prophylactic intramuscular injections (1 ampoule, twice daily) prevent life-threatening states. Intravenous injections of Cardiazol-Ephedrine are, however, expressly warned against in the presence of organic heart disorders in the decompensation stage. *Viar* saw an increase of 8 beats in the pulse frequency in a case of heart-block within 15 minutes after a Cardiazol-Ephedrine injection. He continued the medication during the following days, and, 10 days later, 1 hour after the injection, observed an acceleration of the radial pulse to 80 per minute. *Moga* recommends Cardiazol-Ephedrine in bradycardia due to disordered conductivity (heart-block). *Leak* had a case of profound collapse due to *coronary thrombosis* in which he resorted to the injection of 1 ampoule of Cardiazol-Ephedrine without delay. Pains and collapse disappeared in the space of a few minutes. On the strength of his experience he looks upon Cardiazol-Ephedrine as the most rapidly potent of the many cardiovascular stimulants. *Bontscheff* also mentions Cardiazol-Ephedrine among the remedies indicated in coronary thrombosis

Leschke[1], writing on the subject of acute *alcoholic poisoning*, says that, apart from stomach lavage, the liberal use of analeptics (i.a., Cardiazol-Ephedrine) is a necessity.

De Meuron looks upon Cardiazol-Ephedrine as the best antidote in *scopolamine* poisoning.

II. By arsenic

Against arsenical poisoning *Leschke*[3] recommends injections of Cardiazol-Ephedrine, etc. *Dubberstein* also speaks of his favourable experience with Cardiazol-Ephedrine in arsenical poisoning.

III. By other poisons

For the treatment of *hydrocyanic acid poisoning Mannino* recommends the use of cardiotonics and analeptics, e.g., adrenaline, Cardiazol-Ephedrine, caffeine and in addition also lobeline, to stimulate the respiratory centre.

Martinez had a serious case of *mercury cyanide poisoning* in which he injected 3 ampoules of Cardiazol-Ephedrine intramuscularly. After 30 minutes the patient was practically restored, the entire objective symptomatology having disappeared.

Balázs records several cases of *vanilla ice cream poisoning* successfully treated by Cardiazol-Ephedrine.

Lutfi gave the remedy in a grave case of poisoning by *castor seeds.*

Becmann successfully treated 3 cases of *snake-bite* by intravenous Cardiazol injections and transsternal Cardiazol-Ephedrine injections.

Gusmão has used Cardiazol-Ephedrine, etc., in *jelly-fish poisoning* (physalia pelagica).

fectious disorders (pneumonia) and heart disease. Secondary circulatory lesions also reacted favourably to Cardiazol-Ephedrine treatment. *Petschacher*[1] says that Cardiazol-Ephedrine is the most efficacious remedy in grave, life-threatening circulatory disturbances. According to *Holzbach*, Cardiazol-Ephedrine deserves the preference over all other preparations in *collapse* for the reason that there is no need to inject it intravenously, subcutaneous injections or oral or rectal application serving the purpose. The combination renders particularly eminent services in the precollapse stage in infectious diseases, peritonitis, and moreover also in capillary poisoning. *Abramowitsch* describes the good results *achieved by him with Cardiazol-Ephedrine in collapse. Mayr* likewise makes use of Cardiazol-Ephedrine in vasomotor collapse. *Petschacher*[2] says that it has proved very valuable in shock. *Leschke*[1] writes that the oral or subcutaneous administration of the ready-for-use Cardiazol-Ephedrine combination is indicated in *hypotonic states* (circulatory debility). *Fernández* refers to Cardiazol-Ephedrine as useful in combating hypotonic crises in paludism.

C. Poisonings

I. By hypnotics (and narcotics), alcohol

Risché describes the beneficial action of Cardiazol-Ephedrine in cases of *hypnotic poisoning. Balázs* records a case of hypnotic poisoning in which he employed *Cardiazol-Ephedrine injections* (apart from other medicines). According to *Dubberstein*, Cardiazol-Ephedrine is extremely valuable in poisoning by diethylbarbituric acid and chloral hydrate, poisons which cause lesion of the heart-muscle fibre in addition to vascular damage (see also p. 29).

SURGERY

A. General anæsthesia

I. Before operation

Felsenfeld describes the very satisfactory results obtained by him with Cardiazol-Ephedrine in orthopædic surgery in disturbances of the vascular system as a whole and as a *prophylactic against surgical damage* (collapse, shock). Patients justifying the fear of disturbances during operations were given 1 tablet Cardiazol-Ephedrine or 20 drops Cardiazol-Ephedrine solution twice daily for 3 days before operation. 1 c.c. was administered subcutaneously on the operating table. A further injection was given after operation. Patients received the pre-operative doses also on 4 consecutive days after operation, provided there were no symptoms of post-narcotic cardiac damage. This method proved best to ensure smooth anæsthesia and satisfactory post-operative conditions. In *Felsenfeld's* experience Cardiazol-Ephedrine protects not only the vascular system but the lungs as well. Since he has given Cardiazol-Ephedrine also to patients with defective respiratory organs, he has seen no complications on the part of lungs and pleura. *Nasta* recommends the administration, 1 hour before operation, of Cardiazol-Ephedrine and Dilaudid (Knoll) plus scopolamine (or other additions) for pre-operative medication in gastric surgery. *Stohr* prepares patients of very advanced age and with myocardial damage by the administration of 10—15 drops Cardiazol-Ephedrine, thrice daily. He emphasizes the excellent and prompt action, more particularly on the blood-pressure. Before ether anæsthesia, *Fervers* gives an intravenous injection of a

Addendum: *Coma diabeticum.*

Landabure names Cardiazol-Ephedrine among the remedies indicated for the treatment of coma diabeticum.

D. First-Aid Services

Kese has used Cardiazol-Ephedrine as a respiratory and circulatory stimulant in countless cases of collapse, hæmorrhages, angina pectoris, diabetic coma, asthma attacks and collapse due to poisoning. The administration of Cardiazol-Ephedrine is the first step taken by *Fasal* in cases of serious burns where an alarming general state calls for prompt succour.

E. X-ray malaise

Hug tried Cardiazol-Ephedrine with thoroughly satisfactory results in some 50 cases of X-ray malaise, the favourable effect being due to a raising of the sympathicus tone. *Hug* used no injections but gave the preparation in the liquid and tablet forms, patients receiving on an average 20 drops before irradiation, 1 tablet in the evening and another tablet next morning if necessary. This medication sufficed in the majority of cases to prevent the malaise altogether. *Mursa* gave Cardiazol-Ephedrine in a case of severe crisis after X-ray irradiation and has since used the combination regularly for prophylactic purposes. Cardiazol-Ephedrine is also mentioned by *Gurniak* as one of the remedies used by him against X-ray malaise.

III. After operation

According to *Felsenfeld*, Cardiazol-Ephedrine renders excellent services in chronic circulatory disturbances *complicated by post-operative pulmonary and pleural trouble*, but more especially also in chronic insufficiency of the arteriosclerotic heart. In consideration of the age of such patients he gives 10 drops, thrice daily. In insufficiency of other genesis the combination is equally useful.

Tönnis mentions Cardiazol-Ephedrine among the remedies of value in post-operative *circulatory disturbances* (thrombosis of pelvic veins). *Barboza Vianna* gives the preference to Cardiazol-Ephedrine after operations on children (especially under rectal anæsthesia) and praises its good effects. In serious post-operative circulatory disturbance he first gives Cardiazol and subsequently Cardiazol-Ephedrine.

Linzenmeier and *Wallischeck* have, by the comparative evaluation of blood-pressure curves, established the fact that in patients with peritoneal shock after operations or hypotension caused by much loss of blood, Cardiazol-Ephedrine has a considerably more persistent and more favourable action than ephedrine alone. Whereas the onset of effect and the resultant rise in blood-pressure are about the same, the duration of effect in the case of Cardiazol-Ephedrine is about 2–3 times longer, despite the very appreciable reduction in the active ephedrine dose.

Addendum: *Blood transfusion.*

In blood transfusions *Monteiro* gives the recipients 1 c.c. Cardiazol-Ephedrine 20–30 minutes before the operation.

small amount of morphine (0·005—0 01 gm.). In order to eliminate the risk of a fall in the blood-pressure as occasionally produced by morphine, he always adds 0 5 c.c. Cardiazol-Ephedrine to the morphine solution; in comparison with pure ether anæsthesia this results in ideal pulse and blood-pressure curves showing but little variation. The Cardiazol-Ephedrine addition, moreover, has a favourable influence on the uncomfortable sensations which may follow a too rapid injection of the morphine. The method allows a cutting down of the otherwise customary subcutaneous dose of morphine by one half and the same reduction also in the amount of ether used. The excitation stage is either eliminated or moderated and the product deals gently with the psyche of patients, in a manner similar to basal narcosis.

Eichenberg recommends the prophylactic administration (i.a.) of Cardiazol-Ephedrine in Avertin* narcosis where hypotension is either already present or likely to develop.

II. During operation

Lloret Barber gives the preference to Cardiazol-Ephedrine as a restorative in *incidents during anæsthesia* for the reason that its vasoconstrictor action is more marked than that of plain Cardiazol. *Monteiro* recommends the administration of blood-pressure-raising medicaments, such as Cardiazol-Ephedrine, and blood transfusions to combat *surgical shock.* In incidents during narcosis he restores patients by injections of adrenaline or Cardiazol-Ephedrine, also intracardially given.

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B. Local anæsthesia

I. Spinal or lumbar anæsthesia

On the strength of more than 200 trials, *Amza-Jianu* and *Moisescu* recommend a method of general spinal anæsthesia with Percaine* and Cardiazol-Ephedrine. Both medicaments are injected together subarachnoidally at various heights, whereby any operation area can be anæsthetized. Anæsthetization is more profound and is also accelerated (5—8 minutes instead of the usual 20 minutes) owing to the vasoconstrictor action of Cardiazol-Ephedrine. The injection is performed as slowly as possible and without any admixture of liquor. The light Percaine* solution becomes somewhat heavier by the addition of Cardiazol-Ephedrine whereby diffusion of the solution is counteracted. Anæsthesia commenced after 2—8 minutes. The maximum of analgesia was reached after 20 minutes and lasted for about 2 hours. The method in question ensures constancy of the anæsthetic state and prevents any disturbances in spinal anæsthesia. *Caldas Barbosa* uses the Amza-Jianu method and obtains the same favourable results. He states that anæsthesia is invariably perfect and of long duration. Malaise, nausea or vomiting are of rare occurrence; the corrective effect of the Cardiazol-Ephedrine on the vagus-sympathicus disturbances appears to be even more marked than its action on blood-pressure— otherwise there would be no explanation for the ensuing subjective and objective improvement because the arterial blood-pressure is not always influenced to any appreciable extent. *Americo Valerio* also describes his experience with the Amza-Jianu method. Analgesia was adequate after only 6—8 minutes, affording confirmation of the fact that the vasoconstrictor action of Car-

diazol-Ephedrine materially assists in the development of analgesia. In his view, spinal anæsthesia, correctly induced with Percaine* and Cardiazol-Ephedrine, meets every desire as to safety and easy applicability. R. *Hoffmann* also injects Cardiazol-Ephedrine in spinal anæsthesia with the object of preventing a fall in the arterial blood-pressure. *Angelescu* and *Tovaru* recommend Cardiazol-Ephedrine, etc., for the treatment of the hypotensive syndrome in spinal anæsthesia. Cardiazol-Ephedrine is used also by *Daniel* to prevent hypotonia in spinal anæsthesia in serious and protracted operations. *Martins Costa* likewise treats arterial hypotension during spinal anæsthesia with Cardiazol-Ephedrine. *Wurzel* reports that, in lumbar anæsthesia, the administration of Cardiazol-Ephedrine is followed by an improvement in the blood-pressure.

Ionescu-Miltiade describes the use of Cardiazol-Ephedrine in spinal anæsthesia according to the Amza-Jianu method, but he combines Cardiazol-Ephedrine not only with Percaine* but also with Novocain* and Syncain*, all these combinations giving excellent results. But since he discovered that subcutaneous injections of Cardiazol-Ephedrine given for this particular purpose are practically as active as subarachnoidal injections, he has dropped the latter in favour of the former. The onset of effect after subcutaneous injections of Cardiazol-Ephedrine ensues after 5—10 minutes and endures for about 1 hour. States of shock during operations are always quickly abolished by intravenous Cardiazol-Ephedrine injections. In *Ionescu-Miltiade*'s experience, a prophylactic injection of Cardiazol-Ephedrine 10 minutes before operation is the most efficacious means to raise the patient's power of resistance in spinal anæsthesia. Blood-pressure is maintained at a

high and constant level, respiration remains regular, deep and uniform. *Rocha Maia* also employs Cardiazol-Ephedrine prophylactically against hypotonic crises in spinal anæsthesia. He injects the preparation subcutaneously 10 minutes before induction. With Cardiazol-Ephedrine administered prior to spinal anæsthesia, the sudden sharp fall in blood-pressure has always been missing. The blood-pressure hardly varies, or falls to an insignificant extent only. In no case has there been surgical shock or cardiovascular disturbance. *Romero* records 59 cases of spinal anæsthesia treated with Cardiazol-Ephedrine injections 10 minutes before induction. Blood-pressure control following injection of the analgesic established either maintenance of the pressure or, occasionally, a small increase. *Bravarski* injects Cardiazol-Ephedrine prior to lumbar anæsthesia and reports that secondary effects (headaches and vomiting) have only rarely been observed since patients have had Cardiazol-Ephedrine injections before and after operation. *Montenegro* regards the subcutaneous or intramuscular injection of 1 c.c. Cardiazol-Ephedrine, 30 minutes before spinal anæsthesia, as an excellent means to counteract a fall in the blood-pressure. *Monteiro* combats a hypotonic tendency in spinal anæsthesia with Cardiazol-Ephedrine (i a.) and also discusses the prophylactic use of this combination against the hypotonic sequel. Also *Burlamaqui Benchimol* and *Santos* use Cardiazol-Ephedrine before anæsthesia. They report on 25 cases, 15 of which were spinal anæsthesias. The supporting action of the Cardiazol-Ephedrine injections in these was generally conspicuous. Anæsthesia in the rest of the patients was induced by other methods (epidural, sacral or local anæsthesia with Scurocaine*, or ether narcosis). In the majority of the spinal anæsthesia cases Rhachiscurocaine*, in some, Rhachistovaine*

were used. *Ivan* also gives a subcutaneous injection of Cardiazol-Ephedrine 10 minutes before the induction of spinal anæsthesia and another immediately after. He belongs to those attributing great importance to Cardiazol-Ephedrine as preventing incidents during narcosis. From *Nagy* and *Lazar* comes the statement that in their cases of spinal anæsthesia they have only had very few instances of slight headaches and none at all of other secondary effects since they have used Cardiazol-Ephedrine as a prophylactic. *Bandera* writes that he also employs Cardiazol-Ephedrine with much success for the combating of disturbances during spinal anæsthesia.

Ionescu-Miltiade and *Burghele*, in a case of sudden *collapse* (4–6 minutes after commencement of spinal anæsthesia) injected 2 c.c. Cardiazol-Ephedrine intracardially. Within a few seconds the heart began to beat perceptibly and spontaneous respiration followed promptly. In less than 10 minutes from the beginning of the incident, patient was fully conscious. The authors express the view that in cases of this kind Cardiazol-Ephedrine is well able to take the place of adrenaline.

II. Local anæsthesia

Kraucher records his observations in 16 cases of Percaine* local anæsthesia in which headaches, transient numbness, small and frequent pulse, disturbances experienced by the patients, were promptly abolished by subcutaneous injections of Cardiazol-Ephedrine. *Della Mano* advocates the simultaneous administration of Cardiazol-Ephedrine where patients are prepared for loco-regional anæsthesia by a dose of Dilaudid-Scopolamine (Knoll).

Asphyxia neonatorum

In the treatment of asphyxia in the new-born and prematurely born, *Sandor* uses Cardiazol-Ephedrine (amongst other medicinal agents).

Toxicosis in infants

In toxicosis of infants, *Chiaffarelli* recommends Cardiazol-Ephedrine in doses of 5 drops or $^1/_2$ c.c., administered 3–4 times daily. He gave the remedy also in a case of grave intoxication ($^1/_4$ c.c.). In the treatment of persistent convulsions he makes use of cardiotonics and states that he regards Cardiazol-Ephedrine as of excellent function in that connection (up to 1 c.c., twice daily).

Enterocolitis

In dysenteriform enterocolitis of children, *Lustosa* gives Cardiazol-Ephedrine internally (among other remedies).

Infectious diseases

Rocha enumerates Cardiazol-Ephedrine among the medicaments used by him in the treatment of circulatory insufficiency in acute infectious diseases of children. *Honold* now practically confines himself to Cardiazol-Ephedrine in the treatment of bronchitis and *bronchopneumonia*, especially of infants. $^1/_2$ ampoule is generally sufficient to prevent circulatory failure or to restore an existing subnormal temperature to normal values. *Gavrilă* injects Cardiazol, Cardiazol-Ephedrine, etc., in infantile *diphtheria* against manifestations of vascular insufficiency. *Manicatide* and *Cajal* include Cardiazol-Ephedrine among the medicaments re-

garded by them as valuable in diphtheria where there are signs of adrenal insufficiency (pallor, grave asthenia, feeble pulse, tendency to collapse).

Asthma infantile

(see page 218).

GYNÆCOLOGY AND OBSTETRICS

Operative obstetrics

According to *Tausch*, Cardiazol has been found most valuable as a central and peripheral tonic during lumbar anæsthesia in operative obstetrics.

Circulatory debility after childbirth

Baumgarten records 3 cases of marked circulatory debility after difficult childbirth with detachment of the placenta and hæmorrhage lasting several hours. An intramuscular injection of 1 c.c. Cardiazol-Ephedrine, in combination with 2 c.c. Secacornin* (the latter for the purpose of contracting the uterus), rapidly abolished the manifestations (small pulse, marked pallor, incipient cyanosis). The pulse grew fuller, respiration more active and the face regained its normal colour. In another case the patient had lost about $1^3/_4$ pints of blood with the result of serious general debility. An injection of 1 c.c. Cardiazol-Ephedrine considerably improved the condition within about 15 minutes.

Puerperal fever

Louros employs Cardiazol-Ephedrine in puerperal fever as an addition to intravenous continuous drop infusions.

NEUROLOGY AND PSYCHIATRY

Depressions

In states of depression and anxiety in people of advanced age *Falthauser* has observed beneficial results from the administration of Cardiazol-Ephedrine.

Parkinsonism

Against transient secondary effects of atropine treatment of Parkinsonism (flushing, palpitations, vertigo) *Römer* recommends tinct. valer., Cardiazol or Cardiazol-Ephedrine.

Narcolepsy

Luque reports very good results from the Cardiazol-Ephedrine medication in a number of cases of narcolepsy (1 tablet morning and evening).

DOSAGE

Oral application

The average dosage is 10–20 drops or 1/2–1 tablet Cardiazol-Ephedrine twice to thrice daily. In chronic insufficiency of the arteriosclerotic heart only 10 drops or 1/2 tablet, thrice daily, are given in consideration of the patients' advanced age. Where the blood-pressure is above 200 mm. Hg it is advisable to abstain from the medication.

Injections

Subcutaneous or intramuscular injection answers the purpose best. 1 ampoule is generally sufficient, but 2–3 injections daily may be given if required.

Intravenous injection of Cardiazol-Ephedrine in organic heart disease in the decompensation stage is emphatically warned against.

TRADE PACKINGS

Cardiazol-Ephedrine tablets...... Tubes of 10
Hospital packings of 100

(Each tablet contains 0·1 gm. Cardiazol + 0·015 gm. *l*-ephedrine hydrochloride)

Cardiazol-Ephedrine liquid....... Bottles of 10 gm.
Hospital packings of 100 gm.

(1 c.c. contains 0·1 gm. Cardiazol + 0·015 gm. *l*-ephedrine hydrochloride)

Cardiazol-Ephedrine ampoules ... Boxes of 6
Hospital packings of 30

(Each ampoule contains in 1 c.c. 0·1 gm. Cardiazol + 0·015 gm. *l*-ephedrine hydrochloride in sterile aqueous solution)

Hospital packings are supplied at substantially reduced prices.

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CARDIAZOL IN COMBINATION WITH OTHER MEDICAMENTS

Apart from the combinations described in the foregoing—Cardiazol-Quinine, Cardiazol-Dicodid and Cardiazol-Ephedrine—, Cardiazol can be combined with a great many other substances.

Some of the most important *possibilities of combination*, already frequently referred to in these pages, may usefully be described again in brief summary. *The combinations in question are not marketed as such and require compounding by the chemist on prescription.*

I. Cardiazol combined with digitalis [Digipuratum (Knoll)], strophanthin, ouabain, etc.

(a) Digitalis (Digipuratum)

According to the experiences of *Fahrenkamp* and other authors, the addition of Cardiazol to an ineffective or inadequately effective dose of Digipuratum (Knoll) will impart an unmistakable tonicising action to the glucoside dose. It follows that there is a saving in digitalis glucosides where these two preparations are given for a protracted period but that the reduction in the glucoside dose does not diminish the extent of the action.

(c) Ouabain

Akil Muhtar's observations on the isolated heart of the frog have shown that Cardiazol will reactivate the heart function previously arrested by the influence of ouabain. *Haddad* found that an addition of Cardiazol to ouabain raises human tolerance to the latter very considerably so that the administration of even large glucoside doses ($^1/_2$ mgm.) is not fraught with danger.

Indications for the Cardiazol-Ouabain combination:

Decompensated heart diseases (primary treatment), ventricular insufficiency, arrhythmia and bradycardia. (See also page 49.)

Since the Cardiazol-Ouabain combination is not marketed as such it must be prepared on prescription. *Haddad* recommends 2 intravenous injections daily of 1 ampoule Cardiazol together with $^1/_4$ mgm. ouabain.

Cardiazol can also be usefully combined with strychnine, sparteine, scilla, tinct. convallar., etc.

II. Cardiazol combined with caffeine

The action of Cardiazol is considerably enhanced by caffeine. The strengthening of the absolute cardiac function by caffeine is of importance, apart from the centrally excitant effect on the vascular nervous centre in the sense of vasoconstriction, especially in the important splanchnic region, an action which caffeine shares with Cardiazol.

Indications for the Cardiazol-Digipuratum combination:

Cases requiring protracted digitalis treatment when a reduction of the glucoside dosage appears desirable at the same time. (See also p. 47 and 54.)

The Cardiazol-Digipuratum combination is not obtainable on the market as such. The physician acquires 1 box of Cardiazol ampoules and 1 box of Digipuratum (Knoll) ampoules and mixes the preparations in the syringe, or he gives a prescription for the necessary amounts of Cardiazol and Digipuratum pulvis, liquid or tablets to be taken orally.

(b) Strophanthin

According to *Fahrenkamp*, the simultaneous application of Cardiazol eliminates the undesirable action of strophanthin on the heart frequency. *Hildebrandt* had previously shown in experiment on the isolated heart of the rat that the Cardiazol is able to neutralize the poisoning effect of strophanthin. In human practice, *Fahrenkamp* has, in bradycardia with arrhythmia perpetua, been able to prevent an abrupt decline in frequency.

Indications for the Cardiazol-Strophanthin combination:

Lessening of risks attaching to pure intravenous strophanthin therapy.

Cardiazol-Strophanthin is marketed by Messrs. C.F.Boehringer & Sohne, G. m. b. H., Mannheim-Waldhof, Germany, under the name of Strophanthin. compositum* (ampoules of 1 c.c. containing 0 25 mgm. strophanthin + 0·1 gm. Cardiazol)†.

† Not as yet universally obtainable.

The Cardiazol-Diuretin combinations are not on the market as such. For oral application the prescription is either for tablets [1 tube each of Cardiazol tablets and Diuretin (Knoll) or Calcium-Diuretin (Knoll), Iod-Calcium-Diuretin (Knoll) or Rhodan-Calcium-Diuretin (Knoll) tablets] or for divided powders compounded as directed.

IV. Cardiazol combined with opiates such as morphine, Dicodid (Knoll), Dilaudid (Knoll), etc.

The narcotics of the morphine group and Cardiazol are antagonists whose combined action results in a favourable effect on respiration. Whereas opiates depress the respiratory function, Cardiazol improves (more particularly) the respiratory depth to a marked degree, to some little extent also the frequency; the respiratory volume thus experiences a powerful increase. The Cardiazol addition prevents damage to the respiratory centre also where respiration is normal; such damage is liable to arise from the administration of morphine preparations in aged and debilitated patients especially where the circulation is feeble. On the other hand, the addition of Cardiazol has a favourable influence on disorders in need of opiate treatment and associated with circulatory disturbances.

The Cardiazol-Dicodid combination is on the market in the form of

Cardiazol-Dicodid Drops.

The preparation is exclusively for oral use. (For details see p. 211.)

Indications for the Cardiazol-Caffeine combination:

Heart disease in arteriosclerotics, disorders of the *coronary* arteries or the myocardium, angina pectoris, œdema, collapse of cardiac etiology.

The Cardiazol-Caffeine combination is not on the market *as* such. The two preparations are used in the mixed syringe (Cardiazol and, e.g., caffeine sodium benz., "MBK" amphioles[†]), or Cardiazol + caffeine may be prepared by the chemist on prescription.

III. Cardiazol combined with Diuretin preparations

Diuretin (Knoll), Calcium-Diuretin (Knoll),
Iod-Calcium-Diuretin (Knoll)
and *Rhodan-Calcium-Diuretin (Knoll).*

The combination of Cardiazol with the Diuretin preparations has been found extremely useful in practice. Diuretin (Knoll) dilates *the peripheral vessels as well as the coronary*, cerebral and renal vessels. The preparation raises the entire cardiac output and improves the perfusion of the heart apart from promoting *active diuresis. Indirectly*, i.e., *by improvement* of the circulatory function, Cardiazol also stimulates diuresis and in addition has a favourable influence on vascular spasms, *especially spasms of the coronary* vessels.

Indications for the Cardiazol-Diuretin combination:

Arteriosclerosis with secondary cardiac manifestations (more particularly also coronary *sclerosis, stenocardia and angina pectoris*), dropsy, œdema, ascites, uræmia.

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† Not as yet universally obtainable.

Indications for the Cardiazol-Papaverine combination:

Asthma cardiale and bronchiale, angina pectoris, abdominal vascular crises in arteriosclerosis and tabes. (See also page 53/54.)

The Cardiazol-Papaverine combination is not on the market as such. [1 box of Cardiazol ampoules and 1 box of Papaverine ampoules (Knoll) are used for subcutaneous or intravenous injections.] For oral use prescribe 1 tube each of Cardiazol tablets and of Papaverine tablets (Knoll), 1 tablet of each to be taken several times daily, or write prescription for divided powders, correspondingly compounded.

In the place of papaverine, Octinum (methyloctenylamine) may be combined with Cardiazol.

Octinum (Knoll) is a novel, alkaloid-free antispasmodic, the analgesic effect of which is brought about by an influence on the smooth musculature, excitation of the sympathetic nervous system and a central anodyne action.

The Cardiazol-Octinum combination is administered in the mixed syringe (of Octinum, $^1/_2$–1 ampoule subcutaneously, $^1/_2$ ampoule intramuscularly, pro dosi), or in mixed solution for oral use (Cardiazol liquid + Octinum liquid 1:1).

VI. Cardiazol combined with glucose

The favourable effect on the heart-muscle and vessels of intravenous injections of glucose solution was pointed out by *Budingen* a long time ago. According to *Stejskal*, the intravenous incorporation of hypertonic glucose solution represents an osmotherapeutic measure. This view has been confirmed by *Handovsky*

For purposes of injection, 1 box each of Cardiazol and Dicodid (Knoll) ampoules are required, 1 ampoule of Cardiazol plus 1/2 *ampoule of Dicodid being given in the mixed syringe.*

Indications for the Cardiazol-Dilaudid (or Cardiazol-morphine) combination:

Prevention of disturbances of the respiratory centre liable to occur after morphine medication. Against states of pain associated with circulatory disturbances.

The Cardiazol-Dilaudid combination is *administered* in the mixed syringe [obtain 1 box each of Cardiazol and of Dilaudid (Knoll) ampoules]. For oral administration write out prescription for the desired combination (Cardiazol tablets or solution; Dilaudid tablets). The above also applies to the Cardiazol-morphine combination.

V. Cardiazol combined with papaverine and Octinum (Knoll)†

Papaverine relaxes the entire smooth musculature. The effect of the preparation on the vascular system is confined to pathologically raised blood-pressure, normal blood-pressure remaining *uninfluenced. Cardiazol added to orally administered* doses of papaverine accelerates the latter's absorption and, consequently, action. The property shared by both preparations of relaxing the smooth musculature results in an addition of their effects.

† Known as Octon in the U.K.

LIST OF AUTHORS

and *Meyer* who found that glucose *engenders a change in the* colloidal structure of the blood which alters the responsiveness of the vessels. *Hildebrandt* succeeded in proving that dextrose, moreover, has a very beneficial direct action on the heart. Apart from the latter there is also a distinct effect on the circulation in vascular diseases *(angina pectoris), seen in a lessening of the* angiospastic states.

Indications for the Cardiazol-Glucose combination:

Chronic myocarditis, coronary sclerosis, myodegeneratio cordis, cardiac insufficiency, myocardial lesions after infectious diseases.

An addition of Cardiazol to intravenous infusions of hypertonic *glucose solutions has proved to be of much value* in collapse and it is also recommended for intravenous continuous *drop infusions.*

Cardiazol-glucose combinations are administered in the mixed syringe or given mixed with hypertonic glucose solution prepared *according to prescription* (intravenous infusions or continuous drop infusions).

LIST OF INDICATIONS